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GENERAL ARTICLE

THE USES AND LIMITATIONS OF THE CAPRINIZED VIRUS IN THE CONTROL OF RINDERPEST (Cattle Plague) AMONG BRITISH AND NEAR-EASTERN CATTLE

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SECTION I

1. The Indian Background

To obtain a good perspective of the problem chosen for special treatment in the title of this paper, it is best now to view it against the background of experience accumulated in India upon the uses and limitations of the same method as employed, since 1928, in the field upon the cattle of that country. This is not only because the African experience is more recent, dating only from 1937. In many important ways this more recent African experience has added much to our knowledge. It is mainly because the Indian problem is in some important essentials both less complicated and more complicated; and unless, therefore, the particular problem before us is set upon the Indian picture it may tend to present features to the uninitiated that are blurred and distorted in outline, whereas in reality they blend well with the mellow contrasts of the older background.

The Indian problem is, on the one hand, less complicated because, except for a few imported cattle and cross-breds, which have never acclimatised themselves well to the Indian environment, the races of cattle, amounting to over 120 million head (and not including the buffaloes, *Bos bubalis,* which amount to 30 million head) all belong to the relatively resistant species, or sub-species, *Bos indicus* (the hump-backed or *zebu* breeds). This does not mean to say that they are of uniformly high resistance. As is well known, the different breeds in India vary considerably in their genetic susceptibility to rinderpest; and, as with all breeds, within each breed there are again considerable individual differ-

ences in this respect, as is made evident in the course of epizootics. But, for most part, the various breeds are able to withstand inoculation with a moderately caprinized virus alone, without showing any disturbing clinical symptoms, while, in some breeds, such as the Himalayan hill breed or breeds and the Ongole breed in Madras, the reactions following inoculation with the same virus strain need to be somewhat kept under check by simultaneous inoculation of a relatively small dose of anti-serum. It has come to be well recognised throughout India that it is risky to undertake extensive field immunisation without ascertaining beforehand the probable reactions of the cattle in any given area by preliminary trials. This is well reflected in the successive Annual Reports of the veterinary departments in the several Provinces by the time taken for the new method properly to get under way in each Province. All the same, even when account is taken of the considerable variation in susceptibility of these *zebu* types in India there are none of them, from the extensive experience now gained, upon which the caprinized virus cannot be used in field practice. This was depicted, as far back as 1936, in the following passage quoted from *Agriculture and Livestock Husbandry in India,* 1936-37, issued under the authority of the Imperial Council of Agricultural Research (Delhi, 1939). After passing under review the situation in the several Provinces and Indian States, in all of which the caprinized virus, either alone or, in the case of the relatively resistant breeds, simultaneously with a small dose of anti-serum, had come to replace all former methods of control, the writer says:—

> ". . . The success achieved during the past few years in the control of rinderpest *as a result of the combined efforts of the laboratory and field workers* (my italics), has done much to solve the problem of cattle improvement in this country. Field workers now possess an effective and valuable weapon and can feel more confident in dealing now with this important cattle plague of the tropics, for it is possible now to confer a lasting immunity on any breed at small expense and with the minimum amount of risk. . . ."

Here we must stress that what the writer must have had in mind in making that momentous declaration, long before any similar method had got under way outside India, was that it referred to any breed of cattle actually indigenous to India. Otherwise he would be in grave error.

Another circumstance to which reference must be made in appraising the progress of the new method, and to which allusion has indeed been made in the passage quoted, is that, thanks to the administrative capacity and genius for organisation of the early British veterinary officers in India, there existed throughout that vast territory a framework at any rate of trained field personnel who could be safely entrusted with the working out of the modifications in detail necessary once the principles had been communicated to them from laboratory headquarters and the effective new weapon delivered into their hands. There is no lack of evidence of the vast amount of work that was done in this respect in the short passages in the annual reports of the veterinary departments, which even now has not been properly collated and so is little known outside India.

From the outset of enquiry into possible new avenues, at the end of 1921, the policy had been adopted of keeping the field in the closest possible touch with the prospects opening out before them from inspection of the work in progress at the Muktesar laboratory. At a very early stage, as soon as Kakizaki's researches became known to that laboratory and some tests were carried out there on materials prepared according to his descriptions, it was sensed that immunisation by means of an inactivated vaccine was never destined to succeed in the hands of that personnel. And so it was decided to improve upon the very imperfect serum-alone method, which had reached a state of stagnancy as the sole mode of general field control, early in 1922, by investigating, among the likely avenues of new approach, the possibilities of adaptation of the virus to species other than cattle. The narrative of that episode, as of the subsequent early field developments, has not been collated for publication as the sequence was interrupted by my departure from India in April, 1929. Briefly, it amounted to this: casting around for species other than cattle to which the virus could be adapted, the Muktesar strain was adapted to the rabbit, and studies upon the passaged strain during the next fifteen months showed a definite but irregular "attenuation" in virulence for the local, highly susceptible hill cattle. A disaster then befell that work but for which, if it had not happened, India, perhaps fortunately, in the light of our present-day better knowledge, would never have heard of the "goat-virus." The spread of rinderpest among the goat population of India, resulting from the local manufacture of "goat-virus" at the scene of operations during the early stages of field work, is a contingency for which the present writer,[1] not without some justification, has been blamed. For that spread among a dense goat population which, until then, had hardly ever been known to suffer attack, is, in itself, not a negligible economic setback. A fatal epizootic of rabbit septicæmia destroyed all rabbits in the station, and when means were discovered to circumvent it, it was then found impossible to implant the Muktesar strain again on the rabbit species, not appreciating at that time that that strain, passaged continuously for about thirty years in hill bulls, was a very highly "bovinised" one. Hence, attempts were made to implant it on more easily obtainable and hardier animals, in the shape of the smaller ruminants, again with no better good fortune, until, at last, it was successfully adapted to the goat in November, 1926. During the following months the strain, continuously passaged, whether direct through goats or alternately through goats and cattle, showed such marked attenuation for cattle, all hill cattle, though still showing decided reactions, recovering, and plains cattle (of the Thar Parkan breed, at Karnal, Punjab) showing merely febrile reactions without clinical symptoms, that it was decided, in the first place, to issue goat virulent blood instead of bovine virulent blood for use in serum-simultaneous inoculation.[2] Mysore State had already launched a campaign to control the disease by that method instead of the unsatisfactory serum-alone method, but although the results were highly satisfactory the campaign was costly and great anxiety was experienced at Muktesar in providing supplies of serum of the high potency demanded if widespread accident were to be averted. Moreover, besides, as

had been the practice for several years, valuable imported cattle at the Government Military Dairies and at some other public institutions, such as the Agricultural Research Institute, Pusa, were regularly subjected to immunisation by the double method, but always with much risk, not only from any possible defects in the serum supplied, but also from the onset of piroplasmosis as an accident arising through contamination of the bovine virulent blood used for inoculation. Though an accidental babesiasis could be controlled by careful watching of reactors and prompt trypanblue medication, it was otherwise with theileriasis, the significance of which was then unknown in the country.[3] These deaths of valuable cattle brought down upon the writer severe recrimination from the unenlightened superior authority of the time on the score of negligence, and so, besides the likely but maybe remote prospect of the adapted virus conforming to the Jennerian system, there was the immediate one of allaying frustration in the more widespread adoption of the serum-simultaneous method, for the Royal Commission on Agriculture in India (the Linlithgow Commission, 1928),[4a] on the advice tendered to it, had issued a recommendation that, as one of the primary steps to be undertaken for livestock improvement, the practice of that method ought to be exploited.

The essential principle of the Jennerian system has never been more faithfully expressed, we believe, than in the following passage which is quoted from an address delivered by the late Sir John Ledingham[4] in opening a discussion on Immunity to Virsuses at a meeting of the Comparative Section of the Royal Society of Medicine, London, on April 21, 1943:—

> ". . . In 1936, when opening a similar discussion, I referred to the shortcomings of the inactivated virus as an immunising antigen and *to Jenner's discovery as the 'touchstone by comparison with which all subsequent efforts in this sphere must be judged'* (my italics). The challenge, I believe, still stands. The fact is that there is no royal road to success in this sphere of endeavour and even the triumphs of Jenner and Pasteur offer plenty of scope for further enquiry with a view to betterment. The chief objective must always be the securing of as useful and durable a protection as possible, compatible with safety to the vaccinees, human or animal, and the avoidance of early or remote complications and sequels such as resultant carrier-states leading to fresh outbreaks by contact, insect transmission, or other ways. . . ."

Earler, in November, 1928, communicating to a Conference of the Central Provinces Veterinary Association held at Nagpur, India,[5] the prospects opening out as the result of the work at Muktesar of the preceding six years in alternate host-species adaptation, I had said:—

> ". . . Have we for rinderpest, which we may agree to have in so far as it occurs in India epidemic (or epizootic), features curiously alike to those of human small-pox, means now at hand to adopt a similar policy [to the Jennerian system] of general control? The outcome of recent researches would indicate that we have indeed means that are closely parallel, if not exactly similar, in nature that can be adopted with equal readiness. . . ."

Providentially for India that forecast during the next six years, thanks, as has been stressed, to the initiative and energy of the field workers, turned out to be nearly true. Outside India, however, as was made clear to me in the course of researches upon British cattle at Pirbright from 1940 to 1946, and upon Near Eastern cattle, in initiating a campaign for the eradication of rinderpest in Egypt in 1946 (April-August), the passage quoted, in so far as it embodies the words " with equal readiness," stands in need of considerable amendment. Nevertheless, essentially, the main principle holds quite firm.

It would exceed the limits of this paper to describe how, independently and almost simultaneously, in 1931, in Mysore State (Simpson and Achar), Bengal (Kerr), Central Provinces (James and Stirling) came to discover that the caprinized virus issued from Muktesar could be used alone, without simultaneous serum, safely to immunise the local breeds, the finding being confirmed by direct experiment on a large scale at Muktesar (Cooper),[5a] and how, somewhat later, in Madras (Saunders and Kylsamier) the limitations of the method as applied to the local breeds became apparent, but inoculated simultaneously with a small dose of anti-serum this moderately caprinized strain proved " an excellent outbreak-stopper." Further, we can pass over the several confirmations of the caprinization of the bovine virus undertaken in the Central Provinces (Stirling, Bachan Singh), Madras (Saunders and Aiyyar), Mysore (Srikantaiah) and Burma (Pfaff); the issue of the caprinized virus direct from provincial laboratory headquarters in the form of infected spleen pulp first in Bengal, in 1933 (Kerr and Menon),[6] following upon Haddow's researches at Muktesar, replacing local production of virulent goat blood at the scene of outbreaks; the discovery of the non-communicability of the infection; and how the virus could be employed in actual outbreaks, instead of serum, rapidly and permanently to extinguish them, this being made particularly evident by the experience of Sarwar and Handa,[7] in June, 1934, at the Government Cattle Breeding Farm, Hissar, Punjab, in quelling a serious outbreak at its inception. Again, we need not recount the many reports relating to the durability of protection, which seemed to be life-long, except when the animals inoculated were young calves. Though the massive Indian experience was acquired, readily, by the employment of fresh infected tissue, the rapid progress of the Burma campaign was doubtless facilitated by the issue of the tissue to the field in the form of desiccated spleen powder by Pfaff in 1934,[8] and it is to the credit also of this worker first to have given experimental proof, in 1936,[9] of the very early onset of protection after inoculation with the caprinized strain, thus disclosing what has since become generally known as the Interference Phenomenon.

Viewing the Indian experiences at the present date in historical retrospect, it seems entirely possible that immunisation with a caprinized strain might have got under way, almost simultaneously, in the adjoining territories of French Indo-China and the Philippines, forthcoming from the laboratory observations upon infected goats of Schein and Topacio, respectively. Schein had been led to study the caprine infection through the employment by Yersin

and Krempf, during his absence, of goats for propagating the virus, calves at the time being improcurable.[10] His first conclusions (1917), however were that the virus was unaffected by a long series of passages, even at the 172nd passage the virus still proving lethal for the bovine. Later, however, in 1926,[11] he came to recognise that as the result of divers experiences accumulated since 1920 and reported in some local publications that that early conclusion had been "too hasty," and that the rinderpest virus did indeed suffer attenuation for both cattle and buffaloes by prolonged goat passage. After Schein's death, in 1927, his successor Jacotot did not exploit that observation and became a leading exponent of the use of inactivated vaccines. Topacio,[12] indeed, found that the virus underwent some attenuation for the local Fuga cattle and local buffaloes (*carabaos*) after a single transfer in goats; for the dose of anti-serum required to restrain severe reactions was even at that stage five or six times less than what would have been required had the bovine virus been inoculated. He further suggested the possibility that with continued goat passage the dose of serum could be still lowered. However, he did not proceed with this idea, and spent his remaining years in attempts to "perfect" the inactivated vaccine. We may dismiss Koch's few passages in goats and sheep during his short stay in Kimberley to investigate the great South African panzootic in 1897 as an incident without real relevance in the history of rinderpest control. The possibilities, as we can now appreciate on reading his original reports,[13] and as has recently been correctly stated by Kleine[14] who was an eye-witness of events, were clearly foreseen by Koch himself; but when he visited India immediately afterwards to report upon human plague and was consulted also upon rinderpest,[15] the sole measure he advocated was his "Bile Method," which, indeed, he had been led to adopt from reports given him by Orange Free State farmers. It would be as idle to insist that later work on alternate host adaptation in rinderpest was inspired from the researches of Koch as to contend that those of Kakizaki in Japan with glycerinated vaccine, begun in 1904, Boynton in the Phillipines somewhat later with phenolised vaccine, or of Curasson and Delpy in French North Africa in 1926 with formalised vaccine were all inspired by Koch's discovery of the properties of the bile-inactivated virus. Following largely upon the lines of investigation pursued by the two assistants, Kolle and Turner,[16] whom he left at Kimberley, who early abandoned the Bile Method and concentrated upon the serum-simultaneous method, attention had been deflected generally throughout the world to that method, or where it could not be adopted, as in India, to the serum-alone method. So that by 1922, although there were glimmerings of the possibilities of the inactivated vaccine when Kakizaki's researches became eventually known in 1918,[17] the situation had become so static that a Retrenchment Committee (the Inchcape Committee), appointed by the Government of India in 1923, recommended that Muktesar must be run as a factory for serum production on a self-supporting basis. And in the face of the insistence of authority at the time that those recommendations should be implemented all attempts to explore new avenues were derided and discouraged. Needless to say, Koch's "Bile Method" never stood a chance of even a be-

ginning in India, as anyone familiar with that environment would readly appreciate, and it was with much difficulty and propitiation of Hindu sentiment that "serum-alone" got accepted—a difficulty again which received scant sympathy at the seat of administration. While, except at a few public institutions, the serum-simultaneous method, not only on account of its excessive cost and the risks entailed, but also because it offended Hindu sentiment, made little headway except in the manner which has now been outlined.

Although by 1936 the whole of the main facts regarding rinderpest control by the new system had been worked out in India, the veterinary personnel, as is evident from the departmental reports, becoming fired with zeal and enthusiasm in consequence which is most gratifying to witness after a long period of almost hopeless resignation, and populations and government were eagerly granting facilities to promote extension of the system, the truth remained only too apparent in almost all subsequent reports that progress towards complete eradication had made no great headway; which is the only consideration that need be given to a newer system if it is ever to be adopted in Western countries or in countries like Egypt in replacement of whatever measures are already adopted there.

We need not, for better appreciation of this phenomenon, pass under review developments in the whole of India, but select, almost at random, one of the Provinces, say the Punjab, which otherwise includes several features not unlike the fairly homogeneous feature presented by Egypt, namely, prominently large highly cultivated tracts, the largest of which, reclaimed by irrigation, would correspond somewhat in extent with the whole of Egypt. With a cattle population of about 16 million head, comprising some of the finest draught cattle in the world, like those of the Hariana breed, it has also some potentially fine milking strains, like those of the Sahniwal (Montgomery) and Dhanni breeds. But, unlike Egypt, with its small but dense cattle population of only about one million (besides an equal number of buffaloes), there is also a large mass of relatively worthless cattle, the uneconomic maintenance of which is a sad appanage of the Hindu tradition. Whereas in Egypt no ordinary grazing facilities are available, and the cattle are entirely fed on cultivated crops such as the Egyptian clover (*barseem*) during the cooler months, and then with little or no green fodder, but usually dry fodder in the shape of rice husks during the few hotter months; in the Punjab, however, there is much patchy grazing available outside the cultivated strips, and cattle may wander long distances in consequence. The Punjab also boasts of "the finest institution of its kind East of Suez" in the Government Cattle Breeding Farm, Hissar, where nearly 4,000 head of cattle are maintained, chiefly to supply the districts with good breeding bulls, and on this farm pilot trials of the newer methods of disease control can be readily instituted. There is no lack of excellent public institutions of a similar kind in Egypt, though they are on a smaller scale. In both territories, rinderpest and hæmorrhagic septicæmia are the two most dreaded cattle scourges, the latter sometimes even exceeding the former in importance, though in 1937-38 Punjab report, for example, rinderpest still accounted for 52 per cent of the total death roll. In

both territories, piroplasmosis (babesiasis and theileriasis) and coccidiosis enter into the picture as complications (though, as yet, little is known about the exact significance of bovine coccidiosis in Egypt). But while in Egypt, thanks largely to the strict application of the serum-simultaneous method in the past, rinderpest had, it seemed, been totally eradicated for several years, in the Punjab, on the other hand, the disease is always smouldering in enzootic form within extensive areas, flaring up to epizootic dimensions again within areas in which the "soil" becomes propitious for spread through decrease in number of resistant cattle. The reader is specially invited to consult the late D. T. Mitchell's valuable study, with its excellent maps, of this phenomenon of periodic extension and regression of epizootics from enzootic areas in his Burma Reports from 1932 onwards. Especially valuable are his indications for forecasting regional periodicity of epizootics. The deduction warranted therefrom would be that until 1934 epizootics waxed and waned unhampered by any control measures such as had been applied to them—a state of affairs, as we shall see, which became afterwards transformed after mass immunisation with the Muktesar passaged caprinized virus.

Beginning with the 1928-29 Punjab Report, we learn that following upon the favourable reports from Egypt and Mysore on the use of the serum-simultaneous method, which had been impressed upon its attention by the Linlithgow Commission's recommendations, the veterinary department, admitting no progress had been made in control for (at least) ten years, was considering the prospects of a widespread campaign in favour of the more permanent protection. In the next year, goat virulent blood being then available instead of the previously used bovine virulent blood, it was decided not to delay the campaign; and then, in the following year, 1932-33, we learn that important research work was being carried out at the Punjab Veterinary College, Lahore, in close collaboratoin with Muktesar, the results being most encouraging. A special investigation officer having been appointed to the Province at the expense of the Imperial Council of Agricultural Research, a central body set up on the recommendations of the Linlithgow Commission, trial vaccinations were carried out in different areas, again with quite encouraging results. Then, in 1934-35, large-scale vaccinations were carried out in the Lahore and Jullundur divisions which gave "extremely hopeful results," while at the Hissar farm the use of goat-virus, as already noted, extinguished a dangerous outbreak at its beginning. The spleen tissue vaccine, inoculated alone, as a means of combatting rinderpest, is declared to be a very important advance on the more costly serum-alone method. Next year, 1935-36, the use of the Muktesar goat tissue vaccine is said to have made enormous strides. So much had it gained favour in the Central Punjab where it was first tried in the Province that throughout that circle all outbreaks were being dealt with by the vaccine, 90,668 animals having been vaccinated as against 73,018 in the previous year, while trial vaccinations were also carried out in the Sharpur District of the Rawalpindi Circle. By the next year, 1936-37, the declaration is made that, "Rinderpest can now be effectively controlled at a very low cost with goat-virus tissue," and 169,000 animals were

vaccinated. Animals vaccinated three years previously were found to be still immune to inoculation with the virulent bovine virus. In 1937-38 the number of vaccinations rose to 805,035, the Multan and Rawalpindi Divisions having also adopted the method. Still, serum was employed in 371 outbreaks on 30,511 cattle, either to control severe reactions arising from the goat-virus inoculation, or in cows in advanced pregnancy, or in debilitated animals which could not safely be vaccinated. It is to be regretted that at this moment of triumph the veterinary department lost by the early death of its director, T. F. Quirke, the services of one of our most able veterinary field organisers.

Then, in 1938-39, in spite of the extremely favourable results of the new method of vaccination, we note that 17,241 deaths from rinderpest still accounted for 56.1 per cent of the total mortality. This, it is said, is disconcerting particularly when it is remembered that an efficient and cheap method of prophylaxis is now available in goat tissue virus vaccine. " The fact is, however," the Report continues, " that rinderpest is a disease which though always present in some parts of the Punjab, increases in virulence from time to time and which takes three to four years to reach its peak. One of the chief causes of the appearance of contagious disease in different parts of the Province is the incessant movement of cattle purchased by dealers. A 'stamping-out' policy cannot be applied successfully until control over the movements of cattle is secured through legislation. Some of the District Boards," it is added, " which are alive to this menace, have taken the lead to frame by-laws under Sections 56 and 57 of the District Boards Act of 1883, and it is hoped that other District Boards will follow suit and that matters will considerably improve with the rigid enforcement of these regulations. The department is carrying out vigorous propaganda work amongst the *zamindars* (landowners) to provide segregation enclosures in villages to prevent newly purchased cattle coming in contact with other animals." The total number of vaccinations with the goat tissue virus alone during this year amounted to 695,295 bovines and 1,079 other animals; that is, it was somewhat below that of the preceding year, rather suggesting that the capacity of the department to undertake inoculations had been strained to the utmost. As before, a considerable number was inoculated with the virus in conjunction with serum.

Introducing the report for 1938-40, Mr. Brayne, the Secretary to Government, Development Department, Punjab, says, " The numbers of inoculations and vaccinations of various kinds ran into many lakhs and demonstrate the growing popularity of modern methods of prophylaxis against disease. *Until, however, it is possible to legislate against the movement of diseased and suspected livestock, no amount of vaccination and inoculation will save the province from great and continuing loss from contagious diseases.*" (My italics.) Rinderpest and hæmorrhagic septiæmia together account for 87.4 per cent of this loss. The vaccinations with goat tissue vaccine virus alone amount to 511,923 bovines, with an additional 55,702 cattle and 1,598 other animals in which serum was also employed.

We need not pursue the summary further to gain a clear perception of the

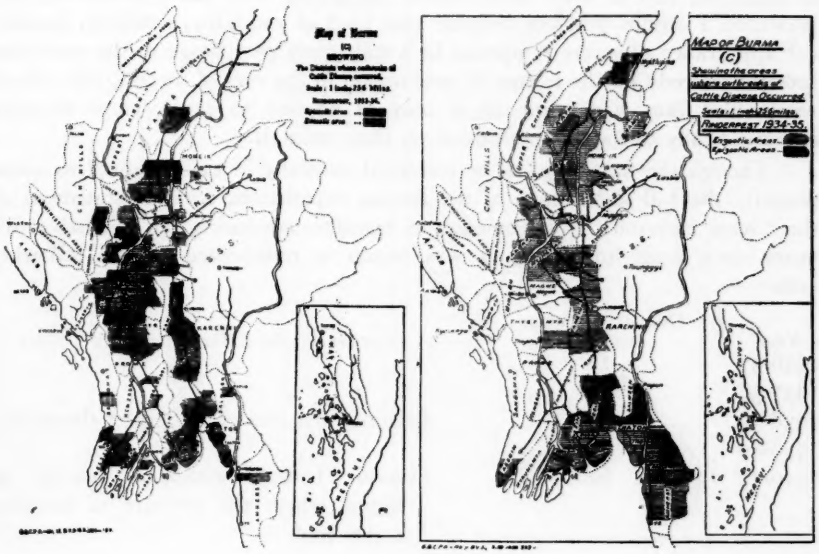
limitations. Partly through inability to undertake active immunization with the personnel available except in areas in which the disease had assumed epizootic features and partly through inability to control movements into other areas, a system of vaccination about as perfect as any human ingenuity has ever devised, had failed in these circumstances to make any profound or permanent impression on the total mortality rate. As has been well said in the Burma reports, it would indeed be difficult in such territories to provide adequate personnel, for the good reason that the disease shows a seasonal as well as a cyclical periodicity, in Burma, at any rate, the season of intense rise in mortality occurring during the months of April to July, corresponding with the onset of the monsoon. Nevertheless, it is clear, on analogy with the well-recognised experience in human smallpox, that unless a very large percentage of the total population is rendered immune, the "soil" remains favourable in which infection can still propagate.

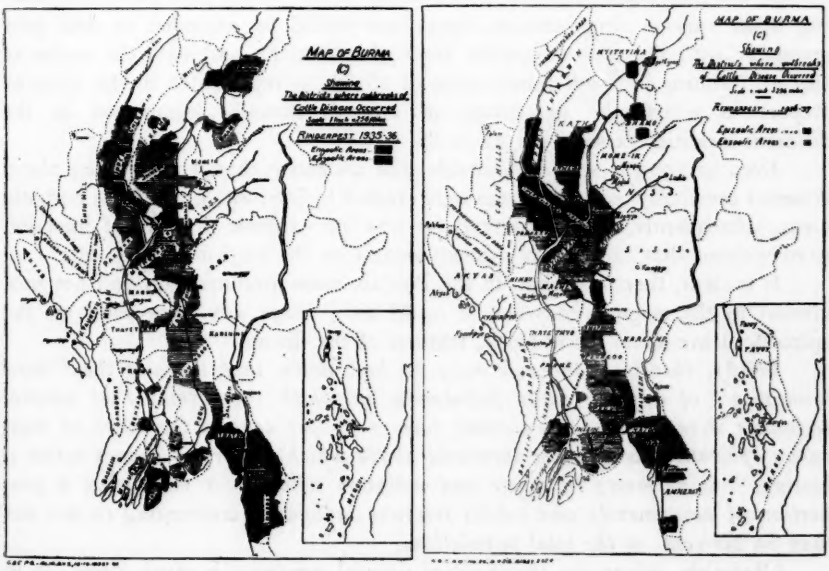
Have we any indication as to the extent to which that "soil" must be transformed before the infection finds it a medium unfavourable for propagation?

Fortunately, we can now gain a very clear idea as to the kind of answer to be given to this question from the Burma experience.

Beginning operations rather later than in India, namely, early in 1934, preliminary laboratory experiments and field trials were carried out during the next two years, so that all was in readiness to embark on a large-scale field campaign early in 1936, the scale of operations being greatly augmented by the issue of the caprinized virus from the outset in the form of desiccated goat spleen tissue. The epizootic and enzootic features of the disease had been extraordinarily well portrayed in previous successive annual reports, and so we are able from the appended charts, on which the epizootic areas are heavily scored and the enzootic areas lightly scored, to gain a vivid impression of the outcome of mass immunisation. Though the country resembles Egypt in the respect that it is a river valley with an upper, dry, region and a lower, delta, more humid, region, the variations in topographical and climatic characteristics are far more intense as are the risks of incursion of the disease from without and the dangers through movement of cattle within. The cattle population, excluding buffaloes and young calves, is roughly $3\frac{3}{4}$ million, and the level of natural resistance can be adjudged from the fact that in the scene of severe epizootics the death rate seldom exceeds 20 per cent. In the marginal hill country, where outbreaks occur relatively rarely, the breeds are highly susceptible. Contrary to Egypt, where the rare appearance of clinical symptoms in the buffaloes, even when the disease is raging among cattle, would give the impression that in comparison with cattle they are of low susceptibility; in Burma, on the other hand, they are of much higher susceptibility than are the local cattle, the death rate in severe epizootics rising to 85 per cent. In India generally, the buffaloes are somewhat intermediate in susceptibility between those of Burma and Egypt, and so present, but not so markedly as in Burma, a rather difficult problem on account of the more severe reactions set up in them than in cattle by a moderately caprinized virus strain. More-

Burma Maps, 1st Set, 1933-1937.





over, whereas in Burma the caprinized strain employed in immunisation caused an accidental death rate not exceeding $\frac{1}{4}$ per cent in cattle, it caused 4 per cent in buffaloes, and in those areas where the species were fairly numerous they presented a serious problem because that level of mortality, entailing, besides, the appearance of severe symptoms in a still larger percentage of the survivors, brought discredit on the system of vaccination in the eyes of owners, who otherwise, when they had witnessed it only as applied to cattle, came forward enthusiastically to have it performed on their animals.

Though the data need to be consulted carefully in their original to assess properly the full significance of the Burma experiences, a crude statement of the "herd immunity" phenomenon as transformed during the successive five years since mass immunization was begun is represented in the following table:—

Year	Overall percentage immunized	Changes in the "Herd Immunity" State
1936-37	10	
1937-38	24	
1938-39	35	Epizootic features of rinderpest disappear.
1939-40	48	
1940-41	62	Enzootic features disappear, except at fringes where the pressure of invasion is very high.

Obviously, at the outset of the campaign, attention would be directed mainly towards suppression of the epizootic zones, while, afterwards, depending upon various circumstances, operations would be extended to deal progressively with the more accessible areas of enzooticity and with the routes of spread, resulting in a differential state of affairs, as represented in the 1939-40 Report in which the percentage of animals actually immunised in the different localities varied from 21 to 88.

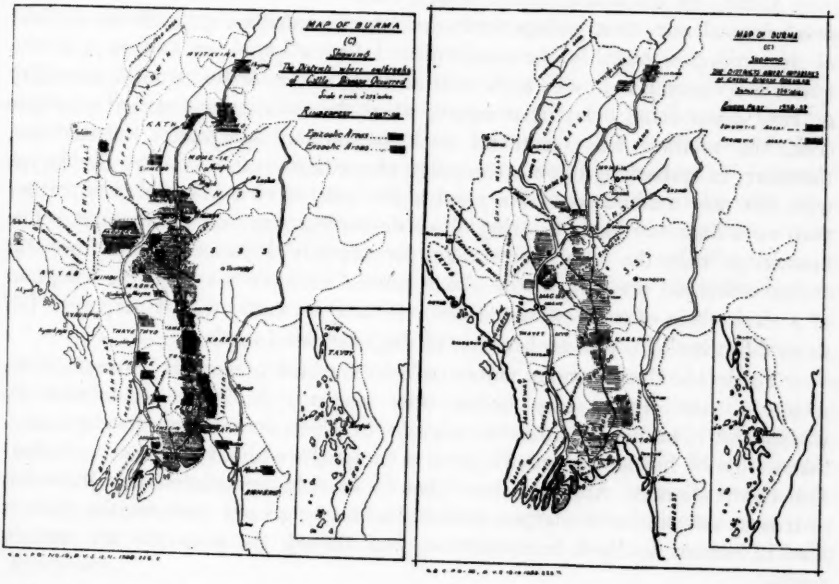
Even in 1939 it was recognisable that an entire change had taken place. Whereas previously, epizootic areas were created by intrinsic spread from enzootic areas, subsequently, on the contrary, it was the extrinsic pressure of infection from without that caused most violent assault on the herd immunity state.

It is clear, therefore, that, in the Punjab, mass immunisation had not progressed to the stage even when it could have made any impression on the epizootic, leave alone the enzootic, features of the disease.

Briefly, therefore, the rule may be laid down that to raise the "herd immunity" of a given cattle population, in which the threshold of natural resistance is represented by a death rate of 20 per cent in the scene of most severe epizootics, to a higher threshold above which rinderpest cannot retain a footing, it is necessary to create and maintain within that population a proportion of permanently and solidly immune individuals amounting to not less than 60 *per cent of the total population.*

Obviously, where the threshold of natural resistance is much lower, as in all races of *Bos taurus,* including the British breeds, in which the death rate

Burma Maps, 2nd Set, 1937-41.



in scene of severe epizootics may rise to nearly 100 per cent, the raising of the threshold will need some corresponding modification.

Again, an important point arising from the Burma experiences is the psychological one, that within territories where rinderpest prevails no method of immunisation ought to be contemplated for adoption, at any rate, at the outset of a campaign, in which the risks inherent in the method entail a mortality nearing 4 per cent; below that figure, when the risks do not exceed 0.25 per cent, the method will commend itself to human acceptance. Better far, therefore, in embarking upon a campaign of eradication in a country like Egypt with this new method to decide upon a low rate of virus establishment rather than on a high one likely to bring down discredit at once on the method. The knowledge that the total percentage permanently immunised need not far exceed about 60 per cent in the above Burma example warrants the adoption of a virus strain of such estimated low virulence for cattle that it may even fail to establish itself in, say, 20 per cent of the inoculated cattle.

To decide these various points calls for careful preliminary investigation, which is not always easy unless their cogency is fully appreciated by administrative authority within the territory in which operations are to be undertaken. To be hustled to embark upon a campaign without adequate investigation courts disaster. And it is here that in its field application the Jennerian system as relevant to rinderpest presents infinitely greater complexities than it does in human smallpox immunisation, even though the principles are entirely similar.

Immediately the Egyptian problem presented itself, therefore, it was clear that the only rational step in the light of the Indian and Burma experience was to render at once as large as possible a proportion of the total bovine population resistant to the disease by means of a *blitz* operation, having most carefully prepared the way on the spot beforehand for pressing forward with it safely and having obtained assurances that there was no lack of personnel.

SECTION II

2. The Measures Adopted in Europe

In Western Europe and in countries generally where adequate stamping-out methods can be applied, rinderpest need never again present a disturbing problem. To any who have had close experience with it, it soon presents itself as a disease infinitely more easy to eradicate than foot-and-mouth disease. Very seldom has it been reported to occur except through a fairly close contact with animals that are actually suffering from the disease, either overtly or as carriers. Our own researches at Pirbright amply confirmed those of many other workers in that they demonstrated the impossibility of transmitting the disease by ingestion of the virus, even when administered in food materials calculated to set up trauma of the buccal mucosa. At Muktesar, no precaution whatever needed to be taken to present spread from the rinderpest area within the station except to keep the cattle tied up during infection in their sheds. It was very much

otherwise always after the incursion of foot-and-mouth disease, which, once it was introduced, could not, in that station, be kept under control.

Tests at Pirbright upon the immunogenic potency of the several body tissues harvested at successive stages of infection and formalin-inactivated confirmed the findings of Kakizaki and his school and of Jacotot and, moreover, demonstrated that during a short phase of the attack the virus exhibited a very well marked selective pneumotropism and this short phase did not synchronise with the enterotropic phase which developed later and was more persistent. Indirect support would thus be given to the recent experimental findings of Idnani[18] at Muktesar, who has found that the infection is transmitted, at an early stage of attack, corresponding apparently with the above pneumotropic phase, at short range only, in the expired breath of an animal when it is suffering from an invasion by an " epizootic strain " of the virus, but not when it is suffering from a milder invasion or from injection with a caprinized strain.

Again, in the outside world, the rinderpest virus shows far greater fragility than does the foot-and-mouth disease virus, this greater fragility in the outside world being due in large part, at any rate, it has been proved, to its much greater sinsitivity to the lytic action of substances, such as animal feeding stuffs, which are endowed with moderate " reducing " properties.[18a] Parenthetically towards certain other reagents, such as formalin, which in slight excess tend quickly to denature the foot-and-mouth disease virus, the rinderpest virus conserves well its antigenic properties even though it becomes equally readily inactivated.

The editorial comments (Leclainche) made in the *Revue Générale de Mèdecine Vétérinaire,* 1920 (p. 577) after describing the history of the last Western invasion earlier in that year are, in this respect, pertinent. That invasion, which was quickly extinguished by " stamping-out " methods alone, occurred after a cargo of Hariana cattle from India on its way to Brazil had been jettisoned at Antwerp and come in contact while in lair with three consignments of American cattle imported for slaughter at various abattoirs. A few, unfortunately before slaughter, came in contact at Ghent with some German cattle destined, by way of reparations, to be distributed among Belgian farmers. The general conclusions drawn from the experience were :—

> " It is clear that rinderpest is not the terrible visitation we had dreaded it to be.
>
> " With some few exceptions, epizootics in the past were observed to arise either in the wake of armies during times of war or else within countries where various obstacles impeded application of proper measures of control.
>
> " The rapid spread of the disease in countries suffering from enemy invasion can be readily understood because infection is then spread by the movements of animals kept under no restraint. The dissemination of infection within countries where State veterinary regulations are difficult or impossible to apply can also be explained. The permanence of the

disease in the East, in Egypt, in India, and the epizootics on the African continent can also be readily explained.

"*On the contrary, the disease can be combatted effectively in those countries which have an adequate veterinary organisation* (my italics.) The 1865 epizootic was eradicated from Northern France without much difficulty by adopting a system that was well conceived but had to be put into operation by such improvised means as were to hand. The spread of that particular epizootic in Britain can be attributed to the fact that the country had then no co-ordinated veterinary service at its disposal.

"The findings made in 1920 are reassuring. They demonstrate the excellence of the classic methods when applied in a country which has available a proper veterinary organisation. It is certain, nevertheless, that the terror inspired by the redoubtable 'cattle plague,' the fearful 'contagious typhus' of cattle, is itself a potent factor in achieving success. It is thanks to this terror that severe measures can be enacted without recriminations and applied without much opposition. The dread of the scourge is such that here the collaboration of interested parties can be elicited and this constitutes a necessary essential for the success of any measure of intervention."

Here the writer was merely re-echoing what had been proved to be true over two centuries earlier, namely, by Thomas Bates, Surgeon to His Majesty King George I, in 1714, and the Papal physician, Lancisi,[19] a little earlier, from their own experiences in successfully and rapidly eradicating the disease; but had been forgotten or overlooked with each succeeding visitation. Hence, too, when I was consulted by the Chief Veterinary Officer (Sir Daniel Cabot) soon after the beginning of the last war in regard to the measures to be taken to deal with possible invasion I had no hesitation in advising him that no outlay need be made for special research beyond what could be easily accomplished as an appendage to the work in progress at the Foot-and-Mouth Disease Research Station, Pirbright. There was no need whatever to embark on such a costly enterprise as was later learned had been undertaken by the Americans with the aid of a body of technologists, with no experience of the natural history of the disease, sequestered on an island.

Explicit in the passage quoted from Leclainche also is the statement that any country which cannot eradicate rinderpest by the classic methods is *not* in possession of an adequate veterinary organisation. An he makes mention in particular of Egypt as wanting in this respect. It was no part of my original mission to Egypt, in April, 1946, to be employed immediately, as I was, in promulgating the newer methods to eradicate rinderpest, but to report upon the educational system which provided such a veterinary organisation for the country. My services were elicited to deal with the grave menace of that disease within the country only after I had placed myself, as was my duty and privilege, at once in touch with the Royal Palace, who thereupon put me in contact with the Minister of Agriculture (His Excellency Hussein Enan pasha) in person, who thereupon deputed immediately his most senior veterinary officer then available

in Cairo (Dr. Makbrouk bey) to wait on me; and it was he who represented that in truth it was the persistence of rinderpest in the country that was arousing really most serious veterinary concern; and my services were thereafter freely given to eradicate the menace. In fulfilment, however, of my original mission an expression of my views, after proper enquiry, was called for during the campaign of eradication, from proper authority, upon the country's veterinary training; and in unequivocal language I had to declare it to be such as is explicit in the passage quoted above from Leclainche. To have minced matters in that grave respect would have been, on my part, plainly a dereliction of duty. The prevalence of the disease since time immemorial, however, was a vagary in the situation that modified profoundly the attitude of the various "interested parties," from the submissive one stated in the passage. In the event, that particular circumstance proved to be the only real deterrent against completion of the campaign as planned.

SECTION III

3. The Behaviour of Caprinized Rinderpest Virus Strains in British Cattle: the Pirbright Experiments, 1940-46

The Pirbright experiences,* insofar as the work was done entirely on British cattle, namely two-year-old Devon steers, discontinued from foot-and-mouth disease research, is of special relevance to the Egyptian problem. For, contrary to what had been long custom at Muktesar, where choice of a highly susceptible bovine for experimentation had been made of Himalayan hill bulls (a well-defined breed, but still of distinctive *zebu* type), in Egypt, on the other hand, it had been found necessary all along for this purpose to import Cyprus bulls, which are of the straight-backed or *Bos taurus* type. Anomalies were therefore encountered during the progress of the work which did not fit in with the Indian experience, two of which need special mention: first, they (the Cyprus bulls) were not "acclimatised" insofar as the prevailing "carrier-states," such as theileriasis and babesiasis, were concerned and so were susceptible to falling victims to the infective agents of these states soon after arrival; and, secondly, in the stricter sense, they were not "acclimatised" to the different climatic and nutritional conditions of their new environment.

Though the term "attenuated" is often, loosely, applied to strains of the rinderpest virus that set up a mild infection in cattle after adaptation to some other host species, it is now well known that some strains of virus can be recovered from mild natural outbreaks of the disease that are actually milder in their effects upon cattle than are some moderately caprinized strains of the virus. Likewise, the term "fixed" goat-virus, deriving from Pasteur's conception of a "fixed" rabbit strain as different from a "street" strain of the rabies virus is, as it were, a label which tells us little about the change wrought in the content of the virus itself. Several workers have now reported that the rinderpest virus becomes "fixed" after about 80 passages in goats; some have not been able

* Much of the earlier work was done in collaboration with J. Francis, B.Sc., M.R.C.V.S. It will be published later conjointly with him in serial scientific papers.

to observe change after much longer passage; Koch in 1897 and Stirling in 1932, besides Topacio, as mentioned above, reported change after a few passages only; while, for the *zebu* cattle of West Africa, which are much more susceptible than those of East Africa,[20] a strain which had been found "safe" for the former was made "safe" for the latter by about 300 further goat passages. Much would seem, from a perusal of the literature, to depend upon the goats that are available for passaging, and, perhaps, on the plasticity of the virus strain selected for passaging. The term "mutant" has now come into use to denote better the kind of transformation that takes place; but again, it tells us little that enables us to perceive the exact change, which, we believe, can now be formulated fairly precisely.

In our experiments at Pirbright, an East African (Kabete) caprinized strain received at the outset of our work was distinctly less pathogenic for British cattle than the Indian (Muktesar) strain received at the same time; though later, in Egypt, the converse was exhibited by the strains received from those two sources.

Some indication of the nature of the changes wrought in the virus during the process of adaptation to a different host-species is given in the following sequence of observations:—

(i) *Serum Immunity.*—With a highly virulent natural bovine strain the dose of anti-serum administered simultaneously can be given in large excess, so as to render the reaction "symptomless"; yet the animal remains solidly immune. With a moderately caprinized strain, the result is usually similar, though occasionally it is found that the virus has failed to establish itself. With a highly caprinized strain, even a small dose of anti-serum is sufficient invariably to prevent the strain from establishing itself in the tissues. Hence, at that stage, the strain obtains a foothold only precariously in the bovine organism, a slight increase in resistance such as is afforded by a mild degree of passive immunity immediately depriving it of such foothold.

These observations tally with those of Green and Carlson[21] working with ferret-passaged distemper virus. Even after only 10 ferret passages they found that the virus could not establish a foothold in the tissues of foxes if the natural, very low, resistance of this species was temporarily increased by passive immunisation. Their published deduction is that "*there is little value in using anti-canine distemper serum in any combination with ferret passaged virus*" (my italics). This statement, by the way, cannot be without grave significance in this country, where, in the current practice of immunising dogs against distemper, veterinary practitioners have departed from the more risky original Laidlaw-Dunkin, or "vaccine-virus" method, and resorted to the more convenient, and apparently safer, "serum-virus" method. It is not unlikely, failing clear evidence of reactions taking place after application of this method, a large proportion, perhaps the majority, of the inoculated dogs are left entirely unprotected. Reading closely that much extolled work of Laidlaw and Dunkin at the present date, however, one cannot but be impressed by its lack of inspiration, which doubtless has led to the present unsatisfactory situation. For

contrary to Puntoni and Green, who quickly appreciated the merits of the Jennerian system (to quote Ledingham) as the "touchstone" in distemper immunisation, those workers failed to do so, although the pointers to it were plain. In that work, moreover, the really onerous task of transferring the results of laboratory enquiry into current and universal field practice was shirked and was thrown over to a commercial firm.

(ii) *Inactivated Vaccines, derived respectively from Bovine and Goat Donors.*—A small dose (2 g.) of formalin-inactivated infected bovine pulp can evoke, for a short time, a very powerful protection in British cattle against a challenge dose of the natural bovine virus. To increase the resistance of these cattle against the severe reactions set up by a moderately caprinized virus strain, a potent vaccine can also be derived by formalin-inactivation of tissues derived from bovines killed at the height of reaction after infection with that same caprinized strain. When, however, goats are employed instead of bovines as donors, the protection evoked is *nil;* but, rather, sometimes the vaccinated bovines on challenge appear to be sensitised so that the reactions observed in them are actually more severe than in unvaccinated controls. This observation falls into line with that of Laidlaw and Dunkin[21a] upon the failure of inactivated infected ferret tissues to evoke an immunity in dogs against distemper. Residence in goat tissues has therefore immediately deprived the rinderpest virus, at least in very large part, of a component which after inactivation, was, for bovines, powerfully immunogenic.

(iii) *The Protective Action, on Bovines, of an Inactivated Vaccine derived from Bovines infected with the Natural Bovine Strain against Challenge with* (*a*) *that same Natural Bovine Strain, and* (*b*) *Caprinized Virus Strains.*—As has been said above, a good inactivated vaccine prepared from the tissues of a bovine infected with the natural bovine virus evokes in bovines a strong immunity against a challenge dose of that same virus. Surprisingly, however, the protection evoked against challenge with the much "attenuated" caprinized virus, even though this virus had been derived from that same virus, as its parent strain, is nothing like so complete as would be expected. Some protection is, indeed, evoked, but it is only moderate. Considering that that vaccine will, on occasion, bring about complete suppression of symptoms in those bovines subjected to challenge with the natural bovine virus, which, if they had been left unvaccinated, as controls, would invariably suffer lethal attack, it is surprising to find the protection to be far less complete in other similar bovines, challenged instead with the caprinized virus, which, if they had been left unvaccinated, as controls, would, for the most part, have recovered from attack. Reciprocally, when the inactivated vaccine was derived from bovine tissues infected with the caprinized strain it was capable of evoking good protection against challenge with that same caprinized strain and a fair protection against the natural bovine strain. It was not surprising to find the Indian and African caprinized strains did not completely overlap antigenically in these experiments, in view of the differences in antigenic relationships already discovered among natural strains by means of the complement function test.[22] But, that a

" weaker " caprinized virus should be more difficult to protect against than its " stronger," lethal bovine parent was unanticipated. It is not, therefore, that in the course of caprinization the bovine virus suffers a total decline in pathogenic status for the bovine, but that it becomes modified in its immunogenic components.

(i) *The Changes produced by Lapinization of a Highly Caprinized Virus Strain.*—In the hope that a caprinized strain which had declined in virulence so that British cattle recovered, though they still showed distinct, but usually not very severe, clinical symptoms, attempts were made to lower its virulence still further by adaptation to rabbits. The results were again unexpected. Repeatedly, at first rabbit passage, the strain lost its capacity to establish itself in the bovine organism; though it still rctained the capacity to infect goats. Recovered goats were then found to be susceptible to infection with the strain as it was before it had been stressed by the rabbit adaptation.

The caprinized virus therefore comprises separate caprine and bovine moieties; and, when a strain is highly caprinized, the two moieties are readily separated under stress, the bovine moiety proving to be a residue which is easily cast off from the preponderating caprine moiety. The two moieties are immunogenically distinct.

The refractoriness of the local rabbits to these infections was overcome by sensitisation, passive sensitisation proving more serviceable than active sensitisation.

(v) *Alternate Rabbit-Goat-Bovine Passage of the Natural Bovine Virus.*—In the hope that it would still be possible to secure the combined advantages of lapinization and caprinization, it was decided to fall back on the parent natural bovine virus. The results proved that soon a phenomenon identical with the above could be induced to appear after a few passages. The strain again " broke," unless great care was taken in passaging to conserve its separate moieties.

It had been our early experience at Muktesar, as already mentioned, as it was afterwards of Nakamura and his colleagues that, though a decrease in virulence for the bovine could be induced by rabbit passage, it was very irregular. Jacotot,[23] on the other hand, was not able to propagate his strain in rabbits beyond a few passages, even after sensitisation, while in our later Muktesar work we had not been able to repeat implantation in the rabbit with the local laboratory strain. Our Pirbright researches revealed that great differences occurred in individual rabbits, so that if a large number were employed at a given passage it would be found that in some rabbits the virus would actually fail to establish itself while, at the other extreme, it would be found that the virus became even exalted in virulence for the bovine organism by residence in a rabbit's tissues. Between thse extremes, an "ideal attenuation" would be found obtainable for the bovine, so that by selection from an adequate number of rabbits at a given rabbit passage it was possible rapidly to obtain a desired " mutant " for our highly susceptible British cattle, which " mutant " had reached a stage of " attenuation " equivalent to that observed in a " highly

caprinized" strain. One more passage of such a strain in rabbits, however, caused it to "break" in a manner identical with that described above when it was a "highly caprinized" strain that was employed at the outset for lapinization.

Whether it is better to employ caprinization or lapinization to secure desirable "mutants," in the light of the above experiences, seems to be an idle question. Whichever method is employed, when the virus has been impressed by heterologous host adaptation to the stage of approximate safety for the most highly susceptible bovines it is in a condition of precarious attachment of the residual bovine moiety within the particulate virus complex.

It would be beyond the compass of the present paper to enter into discussion upon the phenomenon of particle composition of viruses. Knowledge upon its nature is also indirectly derived from studies upon the hæmagglutination phenomenon observed with the influenza and Newcastle disease viruses, and upon the receptor-destroying enzymes which inhibit penetration of the influenza viruses. It is more directly observed by electromicroscopy of the bacterial viruses, or bacteriophages. All these studies enable us to visualise the Interference Phenomenon as occurring at cell surfaces (the monocyte system of cells in the case of rinderpest) where a moiety of particles unable to penetrate the surface block the entry of particles which are capable of attachment, and also afterwards, of penetration. And particles of both kinds may compose a pathogenic virus complex and be in a state of loose attachment as moieties which, under stress, can be detached.

The practical consideration that is here all-important is that one should recognise the stresses that may induce detachment of a residual bovine moiety when it is obligatory to select a strain of the rinderpest virus for immunisation of cattle that possess a low threshold of natural resistance.

This practical consideration may be discussed under the following headings:—

(a) *Relation of Age and State of Nutrition to Susceptibility.*—Contrary to current popular misconception, the host, plant or animal, is in a condition of greatest susceptibility to virus infection when it is in prime condition and in the prime of life; that is to say, when its cell metabolism is most active. Anything which induces a lowering of the cell metabolism, such as faulty nutrition or intercurrent bacterial infection, causes the cell to be less easily penetrated by the virus, and this would evidently become more manifest when the pathogenic moiety within the virus complex is reduced to a small residuum.

The common Egyptian experience regarding the very high susceptibility of the indigenous "calevs"—which are adolescents that have not reached the age when they are drafted for tillage, namely, at three years—conforms with this statement.

It had been our early experience at Muktesar, in laying down tests for assaying the potency of anti-sera, that it was essential not only to select Hima-

layan hill bulls that were outwardly apparently " pure " genetic representatives but also were in the best possible " condition " and vigour, which was evident between the ages of two and eight or nine years, preferably between three and seven. Otherwise, a poor brew might be passed off as a good one, with disastrous consequences when it was employed upon valuable cattle in the serum-simultaneous inoculation.

In our Pirbright experiments, a curious anomaly was frequently observed in employing the high susceptible Devon steers for estimating the concentration of virus in infected tissues, and this anomaly was only resolved by elucidating it from a study in animal behaviour. In the strict observance of quarantine of experimental cattle at the station, the cattle were segregated, usually in pairs, in rows of stone-built loose boxes, and were fed their concentrate ration through a hopper inserted in the wall facing the outside of the compound, the hay ration being fed through the door in the wall facing the inside of the compound. When highly virulent strains were titrated on these pairs, usually the two individuals reacted similarly, but when tissues infected with a highly caprinized strain were titrated, repeatedly it was found that the end-points differed greatly as revealed by one of the pair in each successive box. In the case of an infected goat spleen, for example, the one individual in the series of pairs would indicate an infective concentration at 10^{-6} g., whereas the other at only 10^{-2} or 10^{-3}. It was then noticed that in each box one steer would be the dominating one, standing in wait all day for the delivery of the concentrate ration, which it would devour leaving the other to partake only of what it could of the hay feed. It was the " worried " one of the pair, falling away thus in condition, that needed an infective concentration of virus at least a hundred times as large as that sufficient for the " bully " for the establishment of disease. Even when care was taken to place " worried " individuals only together in the series it happened at once that domination by one over the other brought about a similar phenomenon. Moreover, the experiences showed that separate boxing of individuals was not invariably a good plan as without a partner to " dominate," the cloistered individual tended to " fret."

Such trivial circumstances, as they appear to be at first sight, modify susceptibility so profoundly in working with a strain in which the bovine moiety is at residual limits that in undertaking a campaign, as in a sub-tropical country, where violent changes in the state of nutrition arise with seasonal changes, particularly in unacclimatised animals, they need to be carefully taken into account.

In the case of the foot-and-mouth disease virus, closely similar effects have been studied by us experimentally.[24]

On the other hand, it is also a common experience, particularly in working with goats, and using on them a strain highly adapted to goats, that some " weak " animals may fail to respond by showing any distinct rise of temperature and yet collapse at an early stage of infection and die, showing typical lesions and a high concentration of virus in their tissues. Such animals include females undergoing the stress of lactation. And it is also

well known in cattle that in a mild attack they may collapse at a later stage, with diarrhœa or dysentery, when it is found that the collapse is caused by the lighting up of coccidiosis. Hence, if, as in the case of infection by the lactating goat with a strain well adapted to the goat, the virus succeeds in establishing itself, the body defences may be unequal to offering good resistance to invasion by responding febrilely. In the case of rabbits, although the fever curve is the only guide available to diagnose infection, it was found that the degree of fever gave no sure indication of intensity of invasion, and some which showed no fever were afterwards found to be highly infected.

These observations again are not without relevance in an immunisation campaign where, similarly, cows may fail to exhibit febrile symptoms, yet afterwards, if pregnant, may abort their fœtuses after an interval when it was thought that they had previously scarcely responded.

(b) *Immunisation of Very Highly Susceptible Cattle (Bos taurus types) with Caprinized Strains of the Rinderpest Virus.*—From what has been already said, it would seem that the prospects of obtaining consistent results from the use of strains " attenuated " to the stage when they will be uniformly " safe " and yet still retain the essential property of being able to establish themselves in the tissues of all individuals belonging to the most highly susceptible bovine races are decidedly unpromising. Far better it would seem in practice to select a strain that retains fully the property of establishing itself, such as is evident in a moderately caprinized strain of the virus. To check the reaction provoked by such a strain it would seem that the simultaneous inoculation of anti-serum presents disadvantages. In the first place, it is costly, at the dose required. In the second place, it is difficult to be assured when it is employed at a dose estimated to be fully adequate to check severe reaction that it will not often prove excessive, especially if either in the process of preparation the strain has lost some of its viability or the animal happens to be in a state as regards bodily condition or age when its own resistance is rather high. From what is now known regarding the powerful and fleeting immunity set up in such animals by a good inactivated vaccine it would appear to be better to raise the threshold of natural resistance to a high level with it, and afterwards challenge the immunity at intervals, namely, on the 12th day when it is anticipated to be at its highest, and if the animal does not respond, again 14 days later when it has been found in our work that even a powerful immunity apparent in the 12th day will have waned so that the virus will now gain a foothold but the reaction will not be clinically disturbing. This view would appear to receive support from Daubney's studies[25] in Kenya on the relative merits of serumisation and vaccination as checks to excessive reactions provoked by the caprinized virus. The harvest of inactivated vaccine from a highly susceptible bovine of British breed is so high, when it is prepared according to the simple methods of formalisation prescribed by Colson[26] or Jacotot,[27] from the tissues (tonsils, thymus, lymphatic glands, spleen, and lungs), prescribed by Kakizaki and his colleagues[28] that the yield is certainly an economic one, between 1,500 and 2,000 doses, at 2 g. each dose, having been found to a common yield of potent vaccine.

(c) *" Out-passaging."*—In small-pox vaccination, this has now come to be a well-recognised necessity in the maintenance of " taking " properties in vaccine lymph. In the Anglo-Egyptian Sudan,[29] for example, the vaccine virus is periodically " out-passaged " in local monkeys (*Cercopithecus æthiops*), while in Egypt, the practice adopted at the Serum and Vaccine Laboratory, Agouza, Cairo, is from time to time to interrupt serial transfer in the abdominal epidermis of young buffaloes by using for further transfer in the species lymph from children developing a most pronounced vesicular reaction.[30] This precaution was not neglected in embarking upon the Egyptian rinderpest campaign, when the selected highly caprinized strain subjected to pilot trial upon cattle at a public institution was simultaneously inoculated at the laboratory into Cyprus bulls to provide in part the inocula for the goats destined to yield the materials for field use. Nevertheless, this precaution has not generally been observed by workers, either in India or Africa, who have propagated their strains indefinitely in goats regardless of the necessity. Originally, at Muktesar, as has been already mentioned, two caprinized strains were propagated, one direct through goats and the other alternately through goats and cattle, " mutation " occurring simultaneously with both. But, as has been a common experience with workers, direct passaging eventually resulted in loss of the strain; while in India and Burma[31] no strain has proved, it seems, so satisfactory as the original Muktesar strain in which care was taken to preserve its bovine affinities. When care is taken in " out-passaging " of a highly caprinized strain there is some experience to show that in immunity tests afterwards the proportion of animals found to be immune will be as high as in those animals on which, to ensure " takes," a more pathogenic, that is, only moderately caprinized, strain has been used.

(d) *Preparation of a Strain of Caprinized Virus.*—Hitherto, in all territories, in spite of the low costs as compared with those of all preceding methods of immunisation, preparation has been characterised by gross extravagance and calls now for much improvement. In all our Pirbright work, the simple modification of Greaves's system of desiccation and ampouling devised by Knox[32] for fragile viruses was rigorously followed, using as a protective diluent of the tissue pulp a mixture of heat-inactivated bovine serum (3 parts) and an autoclaved solution of gum acacia, 20 per cent (1 part), usually in the proportion of one part of pulp to four parts of the diluent, the mixture being strained through muslin. " Dry Ice " in acetone was used as the condenser cooler. How long the virus can preserve its activity when prepared in this way we were not able to determine as it seems to be almost indefinitely long. As the stresses imposed on a strain have been proved to vary considerably in the individual animals in which the strain is propagaated, whether goats or rabbits, it is better, considering the potentially enormous yield obtainable from the tissues of a single host, and with the modern methods available for conserving tissues by refrigeration during a test of their properties, to proceed only with the tissues derived from particular donors in which the virus exhibits most distinctly the properties desired after bovine inoculation. Had we been aware of the problem precisely awaiting us in Egypt before departure, it is likely that all the material required for the immuni-

sation of its relatively small cattle population could have been prepared from a single selected British goat [instead of, as afterwards, some hundreds of goats passing through the hands of a mischievous rabble who had to be employed in the work for political reasons].

SECTION IV.

4. Some remarks on the launching of the Egyptian Campaign

Compared with the Indian problem in general and that of the several Provinces and Indian States in particular, the Egyptian problem, so far as its magnitude was concerned, was a minute one, which presented no real difficulties, except the political one, which was represented to me immediately my services were elicited to deal with the problem as one which must be respcted at all costs by the veterinary official put in contact with me. The indigenous cattle, all of high value and often the sole possession of the impoverished peasantry (*fellaheen*) were of the *Bos indicus* type, but genetically, in view of the geographical situation of the country and its history, seemed probable to present marked immunological heterogeneity. So it transpired conspicuously when at public institutions an adequate number of cattle were subjected to inoculation respectively with a " moderately caprinized " and a " highly caprinized " strain of virus. Indeed, that very wide range of variation in susceptibility could well be taken as a delicate indicator of the mixed genetic constitution of those cattle, among which no selective breeding had been undertaken. *A priori,* the threshold of natural resistance, for *zebu* type cattle, was anticipated to be low. For contrary to what has been said about the death rate in severe epizootics occurring in India and Burma, that experienced in Egypt, so far as one could attach any reliability to what was communicated, was high. In an official publication since to hand,[33] to which a rough outline of the preliminary experiments undertaken after my arrival has been appended, the figure of " between 50 and 75 per cent " is given, the rate being highest when the disease appears in a locality after a long absence and is spreading rapidly. Also, it is said, in 1903, cattle inoculated simultaneously with virulent blood and 25 c.c. of an anti-serum, apparently of low potency, produced in Constantinople, suffered a death rate of 90 per cent. This death rate indicated a threshold of natural resistance considerably lower than that of most Indian plains cattle, upon which a moderately caprinized strain of virus can be used alone, as indeed such a strain can be used on those of Assam, the susceptibility of which is estimated to be four times as high as that of ordinary plains Indian cattle. But on the cattle of Madras, as has been said, and on those of the hill country within the adjoining State of Mysore, it would not be safe to use such a strain without serum. While in Himalayan hill cattle and the breeds in the hill tracts of Burma, though their susceptibility does not approach that of British cattle, it would be difficult to undertake an eradication campaign because of the costs entailed in providing the necessary large doses of serum. The question therefore to be resolved at the very outset was whether the cattle of Egypt could safely withstand immunisation even with the most highly caprinized strains of virus or whether, as had been

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the experience with British cattle, it would be unwise to resort to their use. Even though the presence of disease in the country was represented as a most urgent problem, to proceed otherwise than by cautious preliminary experiment to determine these points, even under political pressure, would be culpable temerity. In the Indian provinces generally a preliminary experience in trials lasting about two years had been gained before embarking on wholesale inoculations. Surprisingly, nothing was known about these newer methods by the veterinary official deputed to contact me on arrival.

Egypt had gained a high reputation a few years previously in the control of the disease by the use of the serum-simultaneous method. During the past century, epizootics had occurred in twenty-year cycles, each of the earlier ones lasting about three yars, namely, from 1841 to 1843, from 1865 to 1866, and from 1903 to 1906, apparently through the importation of diseased stock into the port of Alexandria from Turkey, Asia Minor and Nubia. The last of these epizootics, instead of extinguishing itself as in the case of the preceding ones, persisted, in virulent form, till 1912, spreading all over the country, due, it would appear, largely to greater movements of the cattle population, partly to lack of a proper organisation to control spread, and partly also to the fact that the Egyptian buffalo, although it does not often show clinical symptoms after attack, can act as a "carrier." Thereafter, with systematic application of the serum-simultaneous method, the disease lingered but gradually abated in severity, 18 cases only being reported in 1916, and 6 in 1923. Between August, 1912, and July, 1914, 219,000 cattle, representing nearly one-half of the cattle in Egypt at the time, were inoculated by the method, with an accidental death rate not exceeding 1.4 per cent, a figure considered not to be high in view of the presence of babesiasis and theileriasis as complications, though this result was surpassed by that of Mysore (0.69 per cent) from experiences gained with the method in 1925 and 1926, using anti-sera issued from Muktesar at the time.[33a]

There is also a considerable importation annually of cattle from the Anglo-Egyptian Sudan, where the disease is always enzootic, principally for slaughter, but steps have been taken at the frontier (Assouan) to enforce quarantine measures to prevent admission. There is no question but that such veterinary police measures as are being enforced at present in Egypt, such as the closing of markets during local epizootics, have aided materially in the control of the disease. Nevertheless, use had been made continuously of the serum-simultaneous method to extinguish the disease when it appeared in Upper Egypt, apparently through invasion across the frontier. From January, 1923, to March, 1924, it is thus said, 30,000 animals were inoculated in Egypt, with a loss of 91 only, none of which occurred in Upper Egypt, the cattle generally in Upper Egypt, it seems, presenting a higher degree of resistance than those of Lower Egypt.

After a period of quiescence, this method became replaced by immunisation with an inactivated vaccine, as in many other African territories at the time; and in the adjoining Sudan it still remains the method upon which reliance is placed. On my arrival (April 18, 1946), the disease was said to have been

lurking in the country for 18 months, and this inactivated vaccine had proved very disappointing in its use, cattle succumbing to attack even a month after inoculation. Considering that in the Sudan the systematic use of the inactivated vaccine had given favourable results, at least in control, producing a serviceable immunity for at least a year, the failure in Egypt could only be ascribed to one or more of three reasons, namely, unsuitability of donors, improper technique in preparation, or a more fleeting immunity. It seems, indeed, that all three could be impugned. For reasons of supposed economy, Egyptian " calves " were used as donors instead of the more costly, highly susceptible Cyprus bulls. The infected tissue pulp, harvested on the sixth day after infection, comprised a mixture of liver (4 parts), spleen (2 parts) and lymphatic glands (1 part), liver, as is now well known, being a tissue of relatively low immunogenic potency after inactivation. There is also some reason now to believe, as was observed by Lalaune (1940)[34] on the Ivory Coast, that though a high degree of immunity can be induced after inoculation with an inactivated vaccine in the more susceptible races of cattle, it tends to wane in them relatively rapidly.

For Egypt, however, the policy to be adopted must be one of total eradication, which if it cannot be achieved by application of the quarantine measures found adequate to this end in Western countries, could only be expected from adoption of the Jennerian system so as to render such a large proportion of the cattle population permanently immune that the rinderpest virus could not retain a foothold in it. There is now abundant evidence that this goal cannot be achieved by the use of an inactivated vaccine. Three outstanding references can be cited from the literature in support of this contention, namely :—

(a) Cornell and Evans (1937),[35] in Tanganyika, after describing their laboratory studies and field experiences, state that " endeavours to prevent the spread of the disease by vaccinating a ring of cattle around the focus of infection have been ineffective, and found to be a source of danger, owing to the difficulty or impossibility of detecting infection in such partially protected animals." They conclude : " Vaccination [with an inactivated vaccine] should be regarded as a weapon for control of disease rather than as a promising agent for its eradication. For reducing mortality to negligible proportions, and also for preventing the marked loss of condition which the natural disease, or even double inoculation, generally exacts, it is most valuable."

(b) Whitworth[36] describes how for the supply of meat to Singapore, cattle were imported principally from two sources, namely, (i) French Indo-China, where rinderpest is enzootic and the cattle of a relatively high level of natural resistance, but had been vaccinated with an inactivated vaccine (Jacotot) while in quarantine before shipment; and (ii) the Island of Bali, in Dutch Java, which is free of rinderpest, and the cattle naturally highly susceptible. On arrival, in view of the risks, the cattle from the two sources were usually quarantined in separate lairs, but occasionally in emergency they were housed in the same lairs. Repeatedly, rinderpest broke out among the Bali cattle through contact with the vaccinated French Indo-China cattle, which carried the disease in an inapparent or atypical form.

(c) Kakizaki,[37] the pioneer of vaccination with inactivated vaccines, who with his school has probably contributed more exhaustively on the subject than any other worker, describes how, since 1926, across the border separating Korea from Manchuria, the Japanese Government had maintained a protective belt, more than 800 miles long and several miles wide, by inoculating most of the cattle in that belt with his inactivated vaccine. In Manchuria the disease is enzootic and cannot be brought under control. In Korea, however, which had been subjected to annual invasions across the frontier, the disease had been successfully controlled, and the vaccine had proved useful. In spite of the creation of the protective belt, infection trickled through it occasionally and caused extensive epizootics in Korea, as was the case in 1932. This experience contrasts with the recent (1938) well-known African one[38] when the infection was prevented from spreading southwards across the Tanganyika border by creating a protective belt of immunised cattle immunised with the caprinized virus.

Besides the Anglo-Egyptian Sudan, where the prospects of total eradication are remote in view of the extent of the territory, the paucity of veterinary personnel, and the backward state of the country, there are doubtless some special circumstances in which the inactivated vaccine can render useful service; as, for example, in Persia,[39] where the cattle are isolated in groups in widely separated village communities with but little communication between them. As already mentioned, there is also evidence that for the immunisation of very valuable, highly susceptible cattle of the *Bos taurus* types, the raising of the threshold of natural resistance before inoculation with a moderately caprinized strain constitutes probably the most effective form of protection.

One considerable drawback is that for the first three days after inoculation with an inactivated vaccine, even of high potency, the cattle are actually sensitised towards infection; and this may result sometimes in exalting the virulence of a local enzootic infection to the status of an epizootic. This clearly emerged from our Pirbright observations; indeed, there, sensitisation in this way was used frequently to assist a virus in overcoming the resistance of refractory animals.

In any case, for a country like Egypt, with a relatively small and compact entirely cultivated land area, whereon the cattle are somewhat congested, even were the inactivated vaccine employed of the highest potency and inoculated with every precaution having all due regard to its limitations, its inherent defects must condemn it at once for general use in rivalry with an appropriate Jennerian system of vaccination.

Enough has been said already, forthcoming from the Indian experiences, to indicate that the steps in a campaign to eradicate the disease effectively by this system must comprise the following steps always in a new territory:—

(1) Preliminary experiments at the laboratory, upon cattle and buffaloes, representative of the breeds common in the country, to ascertain whether they can withstand inoculation with any caprinized strain without grave risk. If they can withstand it, the further question has to be answered, namely, what strain

ought to be used so as to produce the least risk commensurate with the assurance that the virus has become actually established in the tissues of a sufficiently large proportion of the inoculated cattle. In the case of an immunologically heterogeneous population it is understood that it would be impossible to achieve the ideal of no risk whatever with the certainty of immunity in every individual, and so the aim must be to compromise between the extremes as best as experience and prudence dictate.

(2) Pilot trials, on cattle in public ownership, at Government institutions, of the strain or strains believed from the laboratory results to be most suitable.

(3) Field immunisation. To be carried out with materials precisely as in the pilot trials found to be most satisfactory. Although it would be impossible, in large-scale field work, to take observations upon all animals inoculated, a small number from each large batch inoculated ought to be closely observed, both to ascertain whether, on the one hand, the reactions produced are unduly severe, and, on the other hand, the virus in the inoculum had become inert at the time of inoculation. The results, in either case, should be promptly reported to the laboratory through headquarters. It is obvious that at the laboratory, when it is that freshly prepared tissue suspensions are issued to comply explicitly with the demands of the authority in control of the field staff, it would be impossible to get the laboratory results of tests upon each consignment out in time to give warning to the field.

The very safety of the Jennerian method of vaccination against human small-pox tends to lull the uninitiated into a sense of false security, and lead to neglect in co-operation, hardly realising that good liaison between the laboratory and the field is a first essential in operations where the much more difficult variant of the method represented by rinderpest immunisation is put into practice in a new territory.

In field immunisation, the first aim should be to extinguish any reported foci of infection. No less important — and this proved hard to impress on authority in Egypt—it was immediately afterwards to proceed with the immunisation of the whole cattle population, so as to eliminate any lurking enzootic features and prevent recrudescence of epizootics. An essential condition in eradication, as has now been emphasised in the light of the India and Burma experiences, is that the threshold of "herd immunity" belonging to the TOTAL cattle population should be raised as quickly as possible so that the virus can no longer retain a foothold.

Far more dangerous, as events proved in Egypt, than the hostility, of which there was plenty, against the introduction of the new method, was over-enthusiasm for immediate field application as soon as the early laboratory results became available and before all precautions had been taken to safeguard against possible breakdown.

In addition to what was necessary to be done in the light of recorded experience, it was essential in planning experiments to provide ocular proof, to meet criticism, that the infection would not spread among healthy animals. It was essential too to demonstrate that, besides being non-lethal for the great mass

of the animals, it would not produce in them a distressing loss in condition, even in the most highly susceptible animals, namely, " calves." There was no lack of vehement protestation that these sequels were occurring afterwards in spite of the care taken to allay criticism through demonstrating results at the laboratory. Similarly, again, the contrary position was upheld by another faction, who in turn, in view of the very mildness of the field reactions, and the disturbing phenomenon of the Cyprus bulls at the laboratory with the onset of the hottest weather proving to be unreliable reagents, proclaimed that the materials issued to the field were inert. These two factions maintained their respective clamours. However, the method was pressed on to the stage when at least the disease lost its epizootic features temporarily, and in all important essentials the system derived from the initial planning came to remain, in spite of all ill-advised attempts to improve upon it, the one in current adoption in the country.

Rather, in view of the delicate political position, than employ any strain which had been investigated only at the laboratory and which had not already been put to extensive field use, cables were sent immediately to the chief laboratories in India (Muktesar) and Africa (Kabete, Kenya and Vom, Nigeria), producing strains on a large scale for current field use, to forward by air samples of their most highly " attenuated " strains. Most unfortunately, these samples did not reach Cairo simultaneously, so that the Kenya strain, which was the first to arrive, had been put to a number of experiments before the other two. It was noteworthy that the Indian strain, which was despatched in the form of glycerinated infected tissue, was fully active on arrival, as were the other two, as anticipated, which were received in the form of dried powder.

Briefly, the first results with the Kenya strain showed that although the reactions produced were clinically fairly severe in some of the " calves " and produced fatal infection, complicated with theileriasis in the Cyprus bulls (2/4), the conclusion could be drawn that indigenous Egyptian cattle, contrary to British cattle, could actually withstand inoculation with a caprinized strain. Later laboratory tests with the West African strain (which was a more highly caprinized form of the same Kenya strain) plainly showed that for these indigenous cattle it was more satisfactory, for challenge tests with the bovine virus showed it to have become equally firmly established in them, while the reactions provoked were no more severe than those set up in similar animals inoculated with the Kenya strain simultaneously with 25 c.c. of anti-serum. In buffaloes the reactions were afebrile and symptomless except for diarrhœa in a few (3/8), and death with typical lesions rarely (1/8). This species therefore showed itself to be highly resistant in Egypt, as had been reported. Mature indigenous cattle withstood inoculation, developing only mild symptoms. It would have been decidedly advantageous if these experiments had disclosed that the Kenya strain was quite safe, because the necessary relatively small supplies needed for field use could then have been easily obtained by air. The Vom laboratory was unable to guarantee supplies of the West African strain.

Another laboratory experiment proved that within an enclosure in which the animals were free to move about, cattle inoculated with the Kenya strain

did not communicate infection either to healthy contact cattle or to goats and sheep. Later when naturally infected cattle were introduced into the enclosure, these healthy contact cattle contracted the disease while the inoculated ones were immune.

It would have been of some practical advantage, more particularly, it was said, in countries outside the immediate confines of Egypt, such as the Yemen, if the scarification method recommended by Siddiqi[40] in India could have been employed instead of the subcutaneous route of inoculation. It turned out, however, using it on one-half of the cattle inoculated in the above enclosure experiment, and applying the inoculum to a small scarified area inside an ear in each animal, that this method was dangerous. The reactions were somewhat delayed as compared with those observed after subcutaneous inoculation, but about 60 per cent of the animals died, while none died after the subcutaneous inoculation.

That result accorded well with our own experience at Pirbright, which showed that next to direct inoculation into a superficial lymphatic gland, intradermal inoculation was the most severe route of inoculation. This relative severity can be explained in the light of Henderson's[41] findings also at Pirbright relating to the intimate connection between the skin and the neighbouring lymph-nodes through the connecting lymphatic vessels, so that an intradermal inoculation is virtually an intraglandular one; and, as is now well known, the rinderpest virus has a selective affinity for the monocyte cell system.

The Indian strain, contrary to our experience with a strain derived from the same source in 1940 at Pirbright, proved much milder for cattle than the Kenya strain and even somewhat milder than the Nigeria strain; and had steps not been already taken to proceed with the latter strain it might have been the one selected for field use. It presented, however, it transpired, one undesirable feature, in that there was not complete antigenic overlapping between it and the local bovine virulent strain, two of the 12 " calves " which had exhibited distinct mild reactions after it had been inoculated into them, succumbing afterwards, on challenge, to the local virulent strain showing typical severe rinderpest lesions.

A first pilot trial (June 11, 1946) carried out at the Government Agricultural Station, Sids, Beni Suef, upon 61 adult oxen (6 of which also had received a dose of anti-serum) with the Kenya strain caused such alarm at headquarters when the early stages of the reactions were reported, that it was decided at once to put to trial at public institutions in the same locality, namely, at Minchat Assem, and the S.P.C.A. Beni Suef, the milder, West African strain.

Though none of the oxen inoculated at Sids eventually died, three only suffering from a somewhat persistent loss of condition, it became clear on repeated close examination of the individual animals that the strain employed was too highly pathogenic for general field use in Egypt, particularly when it would have to be employed upon a range of animals, some of which, such as " calves," would exhibit greater susceptibility than the Sids oxen. The reactions observed among the oxen varied enormously, from those which in their earlier stages did not differ clinically very much from those observed in the natural disease to

those in which the response was afebrile, and it was possible, indeed, that in some of the latter the virus had failed to establish itself. However, a challenge test upon five animals later at the laboratory showed that these particular animals were immune. Complicating symptoms, such as those of babesiasis and theileriasis, and in view of the dysentery observed in some, possibly also coccidiosis, were common among the reactors.

From the standpoint of general interest, the most instructive feature of the present communication is afforded by the reactions exhibited by the total of 177 indigenous cattle in the second pilot trial inoculated with the "highly caprinized" West African strain.

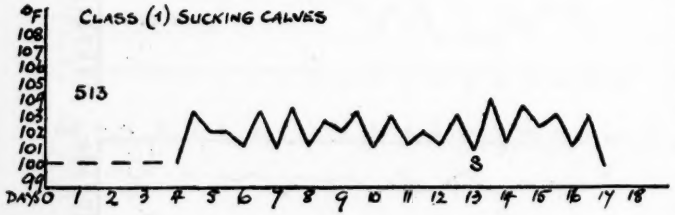
These observations demonstrate the wide range of response that may occur among bovines of the same race, bred in one locality, and inoculated with a given rinderpest strain in which the bovine moiety has been reduced to a small residuum. All had been reared so as not to have been in previous contact with infection.

A few representative charts are reproduced to indicate more precisely this phenonemon, and a summary of the total results is given below, in which, for each class of animal, the reactions are graded: (a) no febrile or other response; (b) very mild febrile, with rarely very mild clinical symptoms; (c) distinct febrile, usually with mild clinical symptoms; (d) severe febrile and clinical symptoms.

		Degrees of Reaction			
Class	No. of animals	(a) Nil	(b) Very mild	(c) Distinct	(d) Severe
(1) Calves at foot ...	3	2 (66%)	1 (33%)	0	0
(2) Weaned calves ...	7	4 (57%)	3 (43%)	0	0
(3) Calves, 1 year old	11	6 (55%)	4 (33%)	1 (9%)	0
(4) "Calves," 2 yr. old ("Steers")	148	59 (40%	47 (32%)	22 (15%)	20 (14%)
(5) Cows	3	2 (66%)	1 (33%)	0	0
(6) Bulls	4	2 (50%)	1 (25%)	1 (25%)	0

All these animals recovered, but in the clinically "severe" reactors, amounting to 14 per cent of the two-year-old "calves," or 11.5 per cent of the total, there was an evident falling away in condition lasting for some time.

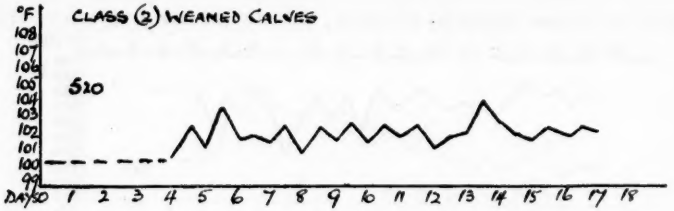
Among the most susceptible group, represented by the above two-year-olds, it was noteworthy that while 14 per cent thus exhibited such severity in response that it would certainly not be prudent to surpass that limit in general field application, 40 per cent, on the other hand, gave no sign of infection. Much former experience had indicated, however, that the virus must have established itself in a fairly large proportion, perhaps one-half or more, of this percentage. So that, were the method to be applied generally throughout the whole cattle population immediately, the "herd immunity" would be raised to the desired level, the permissible margin left for "non-takers" being ample.

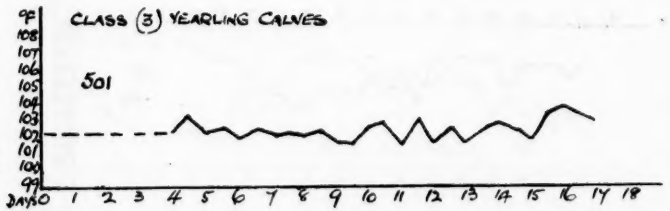


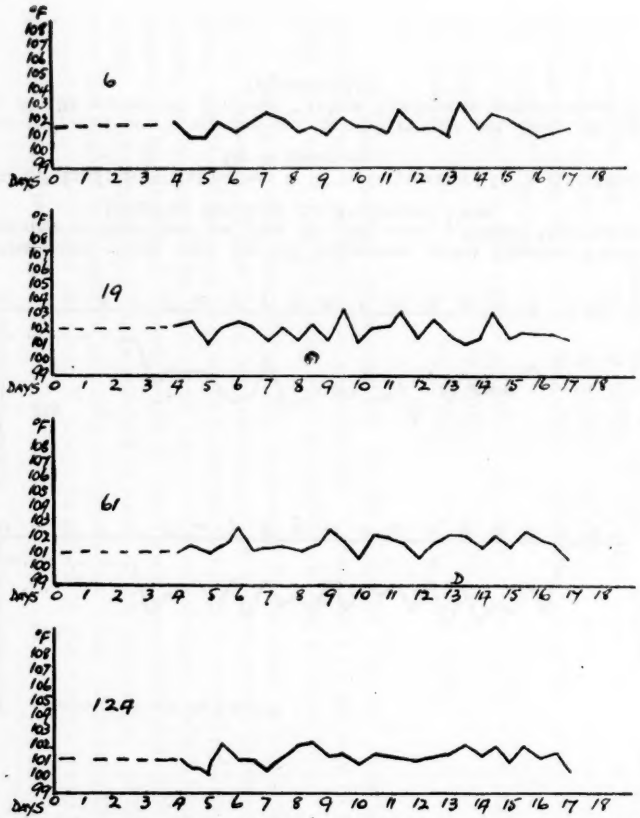
Representative charts from the 177 Indigenous (*zebu*) Egyptian Cattle inoculated at Beni Suef on June 20, 1946, with a Highly Caprinized (Nigeria) Strain of the Rinderpest Virus.

O = off food; S = salivation; L = lacti-rymation; D = diarrhœa; Dy = dysentery.

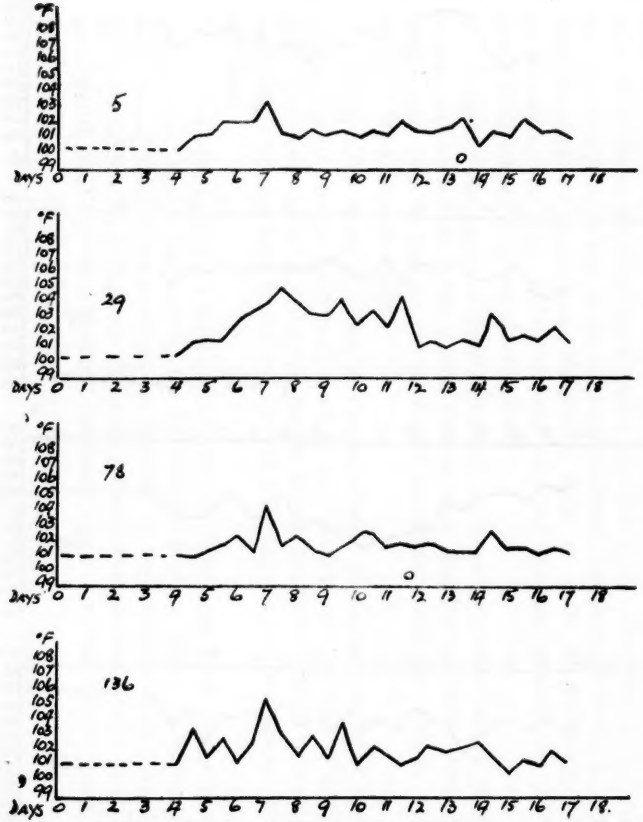
Least and most severe reactors are included in each set, except in the case of the steers (= 2-yr.-old "calves") where a wider range is represented.



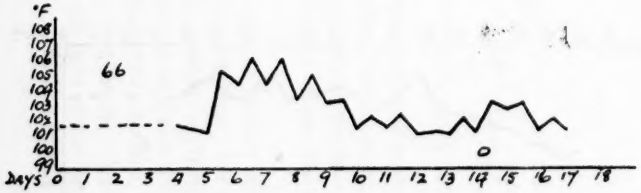


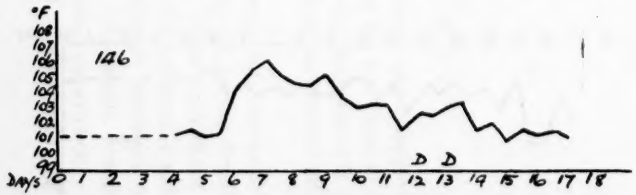


Class (4) Steers (= 2-yr.-old "calves"); (a) degree reactors (= 40%)

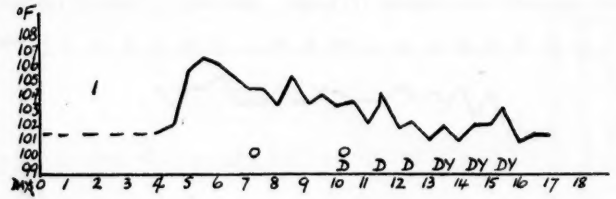


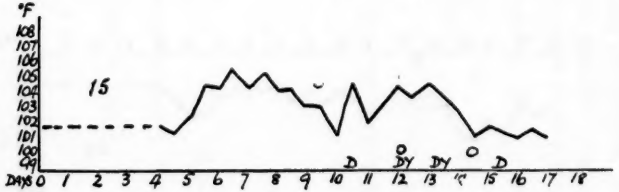
Class (4), Steers (= 2-yr.-old "calves"); (b) degree reactors (= 32%)

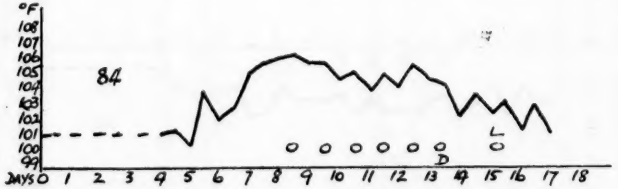


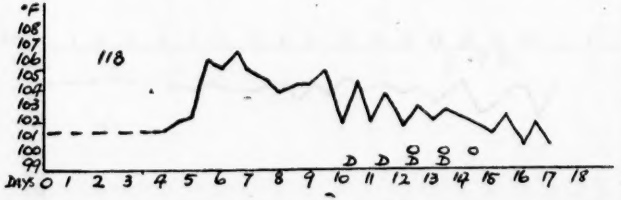


Class (4) Steers (= 2-yr.-old "calves"); (c) degree reactors (= 15%)

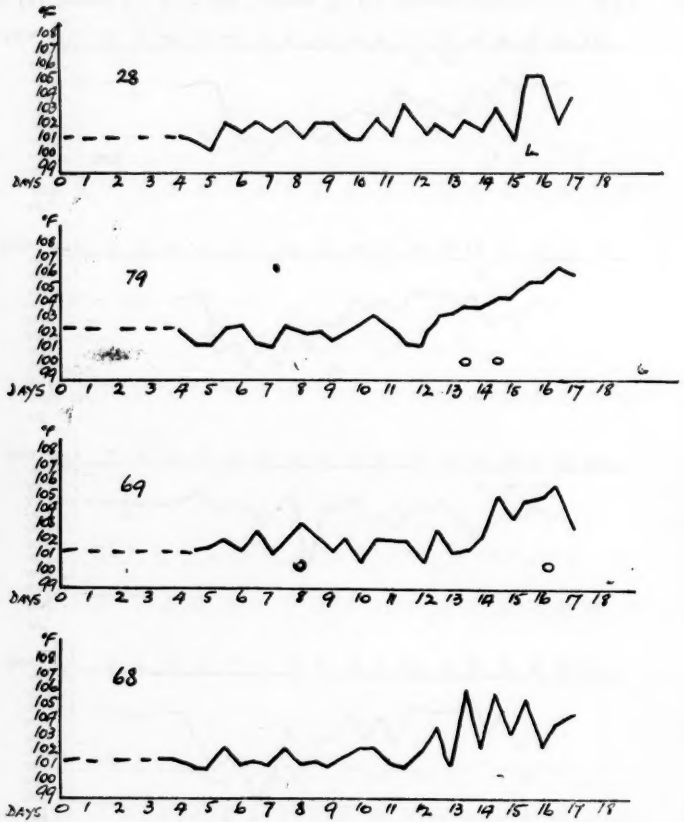




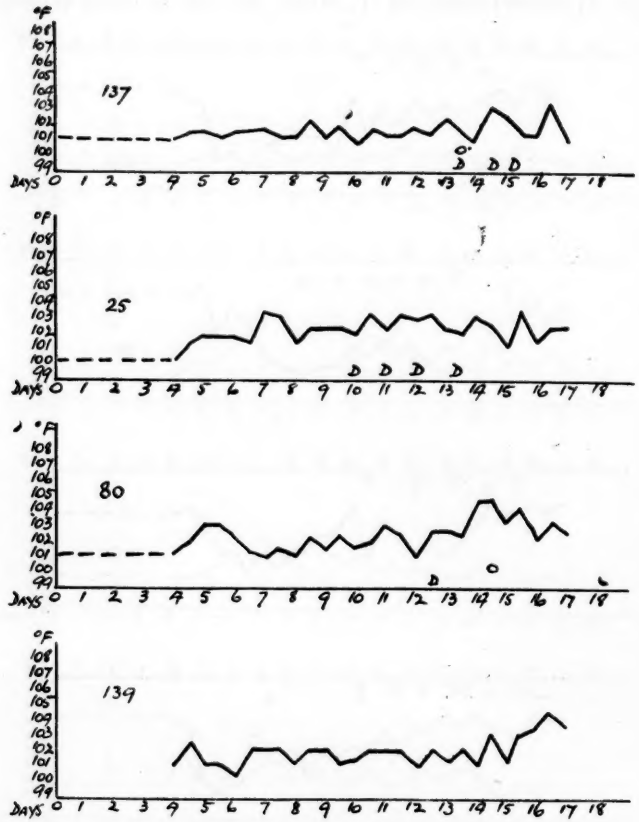




Class (4) Steers (= 2-yr.-old "calves"); (d) degree reactors (= 14%)

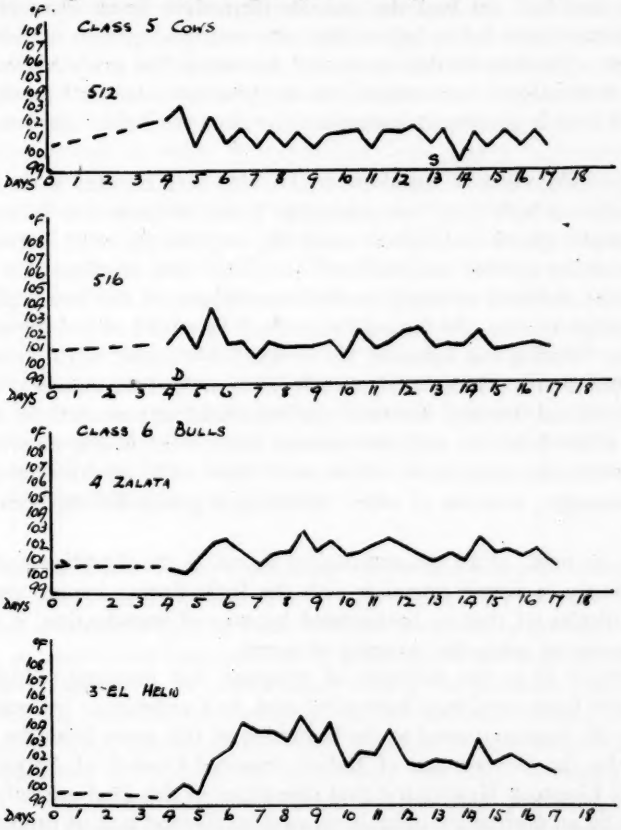


Class (4) Steers (= 2-yr.-old "calves"); atypical late reactions, probably theileriasis sequels.



Class (4) Steers (= 2-yr.-old "calves"); atypical late reactions, probably coccidiosis sequels.

It is also obvious that should the nutritional state of the animals become abruptly changed with the progress of the hot season there would be an increase in this proportion of possible "non-takers." At the outset, however, the new method stood to gain most from a policy of "safety-first."



In the cows, particularly, as has been already mentioned, and is apparent from the appearance of slight clinical symptoms in some of the few cows in the above trial which had shown hardly any febrile response, the fever curve is not to be taken as any sure indication of whether or not the virus has become established in their tissues.

Several atypical reactions were noted, mainly among the two-year-old group, which were probably not true virus reactions, but sequels, taking the form of late reactions, which gave the impression of being either coccidiosis or theileriasis. It had not been our experience in India that the universally prevalent theileriasis was "lit-up" by a rinderpest reaction, though babesiasis and coccidiosis were "lit-up" distressingly frequently. That impression, however, may stand in need of some revision in the light of the Egyptian experience.

Probably no greater uniformity could ever have been secured, in respect of both " breed-appearance " and age and nutritional state, than was presented by the group of 148 two-year-old calves. Yet their response in this trial indicated most marked heterogeneity; so much so, that if one had inspected merely the the charts and had not had the animals themselves under close observation, one might have been led to believe that one was dealing with a wide range of racial types. Entirely similar, as is well known, is the gradation in " takes " displayed in small-pox vaccination, but the gradation does not assume the significance it does in rinderpest immunisation where the " risk " incurred is much greater.

The inoculum used in the above trial having been injected at the laboratory into four Cyprus bulls (for " out-passaging ") and six goats (for " direct passaging), lymphatic gland and spleen materials, respectively, were harvested from the two reacting species, retained on " Dry Ice," and employed for the rapid goat passages, destined to supply pooled immunogen for the contemplated short field campaign to raise the " herd immunity " threshold of the Egyptian cattle population. During the following six weeks (July-August, 1946) nearly a third of that population was inoculated, namely, at or around the epizootic foci, which were extinguished, leaving, however, the remainder unprotected, so that at the beginning of the following year, the enzootic features not having been suppressed, epizootic outbreaks reappeared, which were dealt with, by other hands, by the same immunogen, recourse to other immunogen grades having been met with setback.

Such, in brief, as an epizootiological theme, is the Egyptian lesson, which tallies perfectly in simple essentials with the India-Burma lesson; and, without adequate display of that as background by way of introduction, it would not have been easy to grasp the meaning of events.

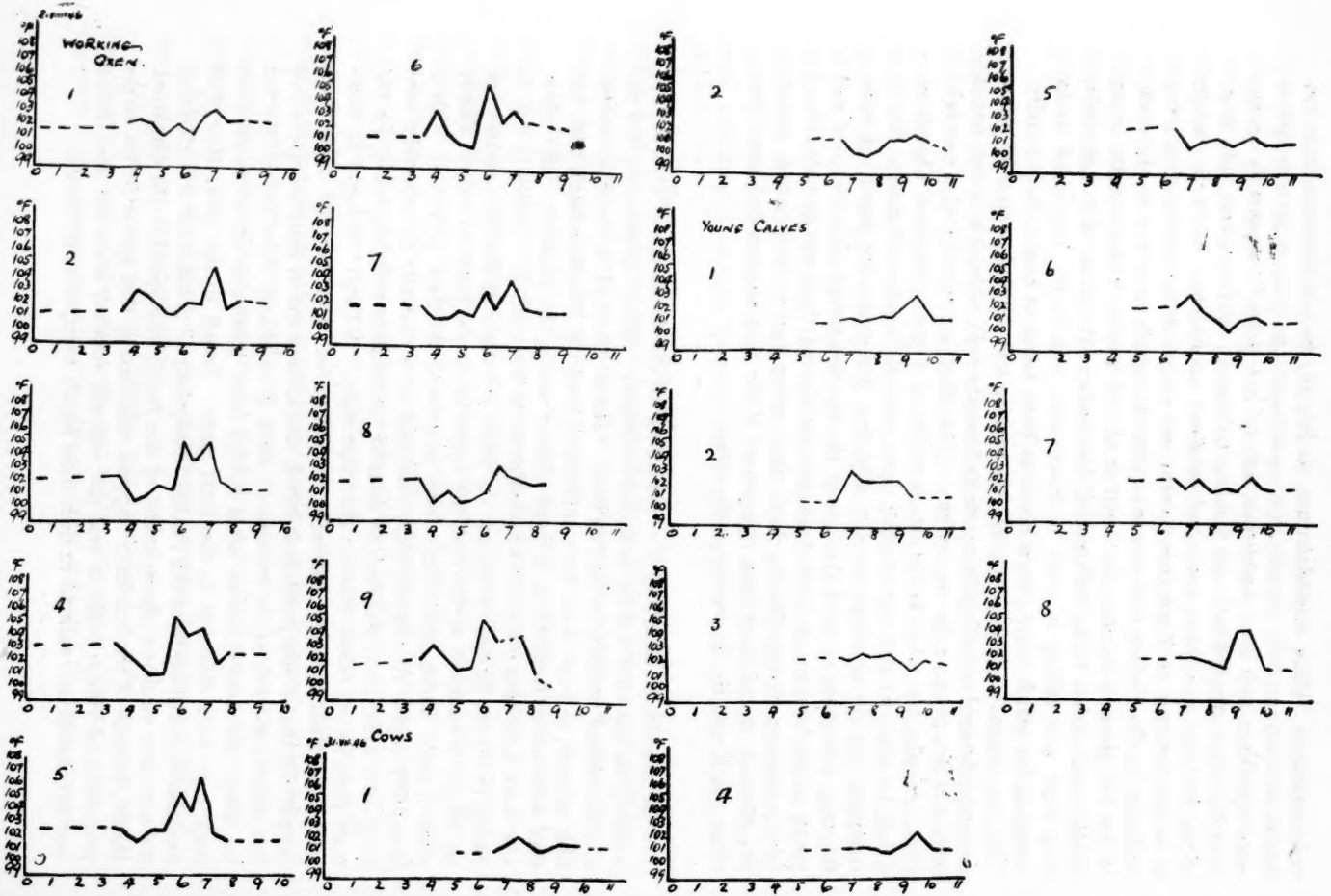
Indeed, it is to the difficulty of grasping that meaning, which grasp is derived only from *combined laboratory and field experience* (as was truly expressed in the passage quoted at the beginning of this paper from the document published by the Government of India's Imperial Council of Agricultural Research and Livestock Husbandry) that operations of this kind are only too often hampered by an obstructive officialdom causing thereby lack of proper liaison—a phenomenon by no means peculiar to Egypt as it had been conspicuously in evidence also in Idia. No praise can be too high for the Egyptian actual field workers, who, like the Indian field workers, on eventually establishing touch with them, readily furnished essential information of the highest possible value and showed acute discernment. It was, as usual, the " interested parties " (Leclainche), entrenched " in office," who blocked, for their own ends, smooth progress.

A few only of the several points of interest emerging from the launching of the campaign are recounted below :—

(a) *Field Checks.*—Much difficulty was experienced in insisting upon the importance of these checks, the early part of the campaign appearing to headquarters to be running so smoothly that doubtless the need for them seemed

over-meticulous. Thus, at headquarters, on July 12, the oral communication was that in the field generally the situation regarding the progress of the new system was " excellent; and, the ' double-inoculation ' is hopeless " (apparently arising from the Cyprus bull donors not yielding satisfactory virulent blood, and thus, in the field, the inoculated cattle had remained susceptible). With the change in season, however, to the hottest months and no proper accommodation being available for the Cyprus bulls under experiment, which were kept in the open, in the full glare of the sun, on desert sand, fed on rice husks, without green fodder, and victims to an outbreak of foot-and-mouth disease and theileriasis, they were now failing to react to inoculation with highly caprinized strain materials for which every precaution had been taken to ensure their activity. This was disturbing, and a temporary suspension was decided upon until assurance was obtained regarding their activity from the field, when it was soon found there had ben no cause for any anxiety. The charts are reproduced of one field check, namely, one taken in the Itsa township of Fayoum province, wherefrom it will be observed that the working oxen were displaying well-marked febrile responses, but the reactions were so mild that tillage was not interfered with, the oxen remaining at work throughout the reaction period. In the cows and young calves, however, as could have been anticipated, there was no well-defined febrile response during the few days' check taken late in the reaction period. No difficulty would have been experienced if the field workers had come into closer touch with the laboratory at the outset.

(2) *Accidental Death Rate.*—According to the testimony of several field workers, the outcome was by no means invariably " ideal," in the sense that the animals reacted similarly to the Itsa oxen. Deaths occurred, in the more susceptible animals, as might have been anticipated from the Minchut Assam trial, but they were not so frequent as to cause dismay among the peasantry, who otherwise were becoming inspired with confidence in the method. During a visit to Assiut, in Upper Egypt, on August 10, while investigating the circumstances of an alleged breakdown at Dayrout, the opportunity was taken to inspect closely about twenty cattle which had been inoculated six days previously with a laboratory issue. Among the older cows and oxen generally the responses were irregularly mild, some showing no decided temperature reaction, while, for the most part, in the others that reaction was slight. A " calf " brought in, however, was showing such distressing symptoms of dyspnœa and high fever (107.6° F.) that it was purchased, killed, and excised spleen material afterwards inoculated into goats at the laboratory, when it was found to be highly infective for them, the natural bovine virus having been previously found to establish itself only with difficulty in the local goats. Issued to the field, after goat inoculation, materials from this further " out-passage " of the strain still exhibited the very low virulence characteristic of the highly caprinized strain employed. Hence, in spite of the indefinite response exhibited at that season by the larger proportion of village cattle, a real risk was still entailed when the immunogen was introduced into animals at their most highly susceptible age-period.



Sample, random, field check. Itsa township (*markes*), Faiyoum province (*mudriya*), on August 5 to 11, 1946.

(3) *Complications.*—By far the most conspicuous and disturbing complication according to the universal testimony of the field observers was the lighting-up of babesiasis ("Texas fever"), acute "redwater" being a common symptom, the proper treatment of which, by trypanblue injection, being, however, well within their knowledge.

(4) *Sequels.*—Again, by far the most disturbing sequel was reported to be abortion, often occurring in pregnant cows which had exhibited hardly any temperature reaction after inoculation. On the King's estate, at Edfina, according to the testimony of an exceptionally shrewd cattle practitioner, Dr. Helmy Zaki Abdel Hai, the King's Veterinary Surgeon, this phenomenon was observed to occur in cows sometimes as late as thirty days after inoculation. However, on the whole this sequel was not very alarming after inoculation with this immunogen, as it would certainly be if one of higher virulence had been employed at the outset in the field.

(5) *"Interference."*—As in India, the field workers, with rising confidence in the application of the method, became emboldened and pressed forward its use into situations which were beyond the original laboratory prescriptions; and, on their own, made important discoveries which only afterwards have received laboratory confirmation. Thus, as in India, they found that the method was actually effective within the scene of an outbreak. At the outset of the Egyptian campaign, the indications deriving from the knowledge then acquired upon the "Interference Phenomenon" were that protection could have been expected after a lapse of about 48 hours after inoculation. In Upper Egypt, however, the Chief Inspector (Diferowi bey) shortened matters by actually inoculating some cattle that were already beginning to suffer from natural attack, and his assurances that this led to an abatement of disease would have been incredible if, afterwards, similar experiences had not been recorded by Green and Stulberg[42] forthcoming from the latters' researches into "interference" by their ferret-passaged virus in warding off distemper in dogs. *"Thus it appears,"* they conclude, *"that a modified virus may be useful for both the prevention and the therapeutic treatment of a disease caused by a virulent strain of the same virus"* (my italics).

(6) *Simultaneous Serum Inoculation.*—As could have been anticipated from our Pirbright researches, simultaneous inoculation of serum into highly susceptible cattle would lead to the complete suppression of the selected immunogen so that it could not establish itself in the tissues. This was made evident, in the course of the visit mentioned above to Assiut, when the temperatures were taken of a large number of Jersey cattle belonging to the American Mission which, on advice from office headquarters, to safeguard them against severe reaction, had each been inoculated with 50 c.c. of serum. None of them reacted. At Talcha, in Lower Egypt, visited two days afterwards, some Holstein-Friesian calves inoculated with the immunogen at about the same time but without serum were showing violent and, in some cases, fatal reactions.

Sample, random, field check. Itsa township (*markez*), Faiyoum province (*mudriya*), on August 5 to 11, 1946.

(7) *Issues.*—To comply with special request, in view of the ready accessibility of all possible scenes of operation, the immunogen was issued from the laboratory ready prepared for field use, the thick suspension of goat-spleen tissue despatched on ice being further diluted down in the field for inoculation, so that each animal receive a dose of 0.01 g. of pooled tissue (5 c.c. of 0.1/500 dilution). Much risk was entailed in such a method, and it is not unlikely that at the beginning some consignments reached their destination inert. Steps had been taken at the outset to improvise apparatus, on the Knox principle, to dry the relatively small quantities required in the campaign; and I am indebted to the Serum and Vaccine Laboratory, Agouza (director, Dr. Mohammed bey Ali) for their active interest in this matter.

(8) *Brucellosis in Goats.*—Care was taken to prevent accidental contamination of the immunogen with brucella, and all goats were tested before inoculation as spleen-donors by means of the agglutination test against *Br. abortis* and *Br. inclitensis.* Again, all spleens were stored on ice before use until they had passed a culture test showing that they were not contaminated. In some consignments of goats, the rate of brucella infection was very high, and this led to the discarding of a large proportion of the spleens. It is evident that if this precaution had not been taken, an extensive diffusion of brucellosis would have taken place among the inoculated cattle.

Acknowledgments

I wish to place on record an expression of my profound devotion and gratitude to His Majesty King Farouk I, who displayed, throughout, the keenest interest in the progress of events and perceived clearly the nature of the difficulties confronted.

Similarly, I wish to express my thanks to the great Egyptian landowner, H.E. Badrawi pasha, of Talcha, for his keen perception of those real difficulties.

Further, my special thanks are due to Dr. Sharaf Eddin, Deputy Director of Veterinary Services, for his loyal support throughout all difficulties; to Dr. Helal Kassem, Divisional Veterinary Inspector, for magnificent observations in field trials; to Dr. Adeeb, Divisional Veterinary Inspector, Beni Suef, for recording the Minchat Assem trials; to Dr. Mohd. Awad Hassanein, of the Serum and Vaccine Laboratory, Agouza, for much fine help and support; to the staff at the Abbassiah Laboratory for continuous work in the hot season and during the fasting month of Ramadan to achieve the beginning reported in this paper; and particularly to Drs. Mohd. Talaat and Hosney Mahmoud, who were able to endure unshaken all the exertions enacted. I have already referred to the excellent response of the field veterinary staff. Finally, I would like to pay special tribute to the present Chief Veterinary Officer of the Ministry of Agriculture and Fisheries, Professor T. Dalling, for his rare insight into the kind of problem presented in this paper and for his sympathy; and to the publishers of this journal (and notably Mr. H. W. Eley) for all the facilities readily given for publication.

Summary

The problem is first viewed against the Indian background, where now an extensive experience has been acquired, which indicates that in a bovine population with a high threshold of natural resistance the "herd immunity" status needs to be raised till it contains approximately 40 per cent of permanently immune individuals for rinderpest to lose its epizootic features, and to above 60 per cent for it to lose its enzootic features. It is this goal which must be reached to eradicate rinderpest in those territories where rinderpest cannot be eradicated for want of an adequate veterinary organisation to apply "stamping-out" measures. Vaccination by means of inactivated vaccines, though sometimes serviceable in control, cannot render achievement of the above goal possible. The goal can only be attained by application of the Jennerian system, which in relation to rinderpest presents infinitely greater complexities than it does in the case of smallpox vaccination, though both are based on essentially the same principles.

It seems impracticable to obtain a strain of virus by caprinization that will be both completely safe for and surely establishable in British cattle and, presumably, all other races of *Bos taurus*.

Under stresses inflicted upon it, of the kind described in this paper, a *highly* caprinized strain readily loses its residual bovine moiety, the main caprine moiety proving to be immunogenically different.

To immunise such highly susceptible *Bos taurus* races, the best plan seems to be to raise the threshold of natural resistance temporarily by inoculation with a properly prepared inactivated infected tissue pulp, derived from the bovine and not from the caprine organism, and to follow this up (in12 days) by inoculation with a *moderately* caprinized strain of the active virus, this to be followed up again by a second inoculation (in 14 days) of the same strain if the animal has not responded.

The main features of a recent campaign to eradicate rinderpest in Egypt are described. The cattle population there, which are of the *Bos indicus* ("*zebu*") type, and thus more resistant than those of the *Bos taurus* type, withstand immunisation with the caprinised virus, which can therefore be employed in eradication. The threshold of natural resistance in the cattle is, however, considerably lower than is generally that of most "*zebu*" races in India, and hence they demand the use of a strain more highly caprinized than are the strains found to be safe in field use for those races as well as those of East Africa. The caprinization needs to be advanced to the equivalent of that required for the West African (Nigeria) races. The use of a strain modified thus far so to contain the bovine moiety merely as a small residuum presents special problems in taking all the precautions that are necessary to ensure that it can establish itself in a sufficient proportion of the *total* cattle population to raise effectively the "herd immunity" to the desired status.

The results acquired in the initial phases of the Egyptian campaign conformed entirely with the epigootiological principles deduced from the India and Burma experiences.

A remarkably close similarity is becoming evident between rinderpest and canine distemper in respect of the complexities observed to arise in devising surely effective and safe means of immunisation.

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REVIEWS

Britain Can Breed It, Farmer and Stockbreeder, Ltd., Dorset House, Stamford Street, London, E.C.1. Price: 12/6 net.

Britain has been called the nursery of the livestock of the world. This is true, but the bold statement should be qualified a little by adding an adjective. It would then read . . . of the *best* livestock of the world. No doubt the climate and environment of these islands has had much to do with the high standards that have been achieved, but one must not forget that we also possess the best stockmen of the world, and the care and management of animals is almost second nature to the average Briton.

Through the foresight of our forebears, who took the first steps to improve the nature breeds, stabilise them and adapt them for particular environments and functions, we have stock of such variety and quality that the needs of almost any part of the world can be fulfilled and to better advantage than with their own nature breeds. In other places, British stock can be used to up-grade nature animals.

For many years our export trade in animals has been good, it can be made better, and one of the ways to do this is to let our customers know what we have to sell. In this way this book has been published at an opportune moment. There are excellent pictures of champion examples of each breed, be they horses, cattle, sheep or pigs, and further a brief historical account is given of each breed, its performance and capabilities, and the chief points which distinguish and typify each animal is set forth. To the foreigner the book will be an excellent guide and its repercussion should be to enhance our export trade, but we are also sure that to many of our own people, even those counted as experts, the book will be a revelation.

Œstrogenic Effects of Subterranean Clover (*T. Subterranean L. Var. Divalganup*): Protective Action of Androgen in the Castrate Male. East, June, Underwood, E. J., Bennetts, H. W. (1949), *Australian J. Exp. Biol. and Med. Science*, 27, 105-113.

The œstrogenic effects arising from the ingestion of a strain of Australian subterranean clover are manifested clinically in sheep by female infertility, maternal dystokia and prolapse of the uterus, and histologically by cystic changes in the endometrium and other abnormalities in the uterus. Castrated male (wether) sheep depastured on this subterranean clover exhibit squamous metaplasia of the secondary sex organs, particularly of the bulbo-urethral glands. The presence of an œstrogenic substance has been demonstrated in ether extracts of samples of subterranean clover from "affected" pastures.

A feature of this breeding problem is that entire male sheep are quite unaffected by the ingestion of "potent" clover, and in explanation it has been postulated that the androgen produced by the testicles was adequate to protect the ram against the effects of the œstrogenic substance present in the clover. Experimental confirmation of this hypothesis is now given in the work described in the present paper.

The results show that in the case of wethers the intramuscular injection of 20 mg. of testosterone propionate ("Neohombreol" Organon) three times weekly gave complete protection against the œstrogenic effect of pasture which was sufficiently "potent" to produce marked pathological changes, characteristic of œstrogens, in untreated wethers maintained under the same grazing conditions. A high degree of protection, not quite complete, was similarly afforded to guinea-pigs by injections of 1 mg. testosterone propionate given on alternate days.

N.J.S.

The Bloodstock Breeders' Review, Vol. XXXVI. The British Bloodstock Agency, Ltd., 26, Charing Cross Road, London, W.C.2.

As each year this wonderful annual comes to hand your reviewer experiences very mixed emotions. Firstly, he knows that within its pages there are many hours of pleasure and instruction; secondly, there is amazement that such an amount of factual information can be encompassed within its pages; and thirdly, there is trepidation for he knows that a review is expected, and no matter how he procrastinates that review has somehow or other to be produced.

The scope of the book is so wide, for it deals with the thoroughbred not only in this country but in many other parts of the world, and it contains such a mass of statistical detail that one might find it easier to review the *Encyclopædia Britannica*. My task is not an easy one, and I will not attempt detail. This is a book which can, and will, provide hours of pleasure to all who are

interested in the thoroughbred, amateur or expert, and certainly those whose livelihood depends on thoroughbreds cannot afford to be without it.

The format is good and the illustrations, of which there are many, are excellent. Amongst the "Memorative Biographies" there is one which all will read with sorrow. I refer to that Ernest E. Coussell, one of the founders of the Review and who bore the major burden of editing over many years.

There have been few who could equal his profound knowledge of the thoroughbred or who were gifted with his facile pen and charm of manner.

NEWS

CONFERENCE FOR VETERINARIANS, OHIO STATE UNIVERSITY

On June 15-17, the Eighteenth Annual Conference for Veterinarians was held at the College of Veterinary Medicine, Columbus, Ohio, under the chairmanship of Dr. Walter R. Krill, Dean of the College. Nearly 400 veterinarians attended the meetings; the papers given covered a very wide range of subjects of interest both to practising veterinarians and research workers. The conference was part of the Diamond Jubilee Celebration of the Foundation of the University. A banquet was attended by many notable personalities of the university, including the president, Mr. Howard Bevis. At the banquet an extremely illuminating and erudite talk was given by Dr. J. A. Myers, head of the Division of Internal Medicine, Medical School, University of Minnesota; the address was an outstanding one of its kind, and dealt with "The Contributions of the Veterinary Profession to Public Health." It was marked by the high praise from an eminent medical worker of the efforts of veterinarians in controlling animal diseases, which have had important repercussions in reducing the incidence of many human diseases. Many of the implications dealt with are, perhaps, rarely appreciated, and it is an address that could be read with profit by many medical workers, whether in research, public health or practice.

The papers given at the meeting included the following, and were distributed in the form of a small booklet to those in attendance. A limited number of these are available on request. (Dr. R. E. Rebrassier, College of Veterinary Medicine, Ohio State University, Columbus, Ohio.):

"Feeding Dairy Heifers," C. F. Monroe; "Sub-Typical Hog Cholera," Fenstermacher and Kernkamp; "Vibrionic Abortion in the Bovine," C. R. Diesem; "Avian Cecal Coccidiosis," F. R. Koutz; "Canine Distemper Infection and Encephalopathies," J. R. M. Innes; "Feeding and Management of Dairy Cattle," W. E. Krauss; "Fundamentals of 'Metabolic Disturbances' of Dairy Cattle," J. W. Hibbs; "Importance of Nutrition and Management on the Performance of the Breeding Bull," G. W. Salisbury; "Feline Restraint and Medication," W. A. Young; "The Contribution of the Veterinary Profession to Public Health," J. A. Myers; "Beef Cattle Practice," F. B. Young; "Swine Obstetrics," F. B. Young; "Zoological Park Veterinary Problems," L. J. Goss;

" Listerellosis in Cattle and Sheep in Ohio," V. L. Tharp; " Demodectic Mange of Cattle," H. E. Amstutz; " Foreleg Paralysis in the Canine," M. W. Allam; " Perineal Herniorraphy," M. W. Allam; " Vibrionic Dysentery of Swine," C. R. Cole; " Important Essentials in Dairy Cattle Nutrition," J. K. Loosli; " Feeding the Milking Herd," C. F. Huffman; " X-Disease in Cattle," J. H. Gainer; " Toxicology in Canine Practice," J. C. Munch.

READERS of the VETERINARY JOURNAL will be delighted to hear that Dr. J. R. M. Innes, who has recently been working at the Chemical-Biological Co-ordination Centre of the National Research Council, Washington, D.C., U.S.A., and holding the post of Research Associate, has been offered, and has accepted, a Special Research Fellowship for one year awarded by the U.S.A. Public Health Services Division of Mental Science. He takes up his new post on August 1 at the Microbiological Institute, National Institutes of Health, Bethesda, Maryland 14. Dr. Innes will be able to continue his researches into the problems associated with demyelinating diseases.

His research projects are:

(1) To follow up some work which has been done on the use of homologous and heterologous brain emulsions with the aid of adjuvents in producing severe demyelinating encephalopathy in monkeys and guinea-pigs after only one injection. This work will have a bearing on the encephalitis which is so common in dogs in America following anti-rabies vaccination.

The work may also have some bearing on the pathogenesis of swayback in sheep. The experimental work will be done on sheep, lambs and dogs.

(2) He will also investigate the pathology and pathogenesis of virus diseases of dogs and ferrets, with particular reference to the encephalitis problem.

Dr. Innes can be congratulated on being offered a special research scholarship which is normally limited to medical workers, and we in this country are proud that an English veterinarian has been so honoured, and wish him every success in his new post.

Publishers' Notices

THE BRITISH VETERINARY JOURNAL, with which is incorporated THE VETERINARY JOURNAL, is published monthly, and copy for advertisements should be in the hands of the publishers—Baillière, Tindall and Cox—not later than the 20th of the preceding month, if proof is required. Tel.: Temple Bar 3386.

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